DEVELOPMENTAL CHANGES IN RESPIRATORY MECHANICS AND BREATHING STRATEGY IN THE GROWING HORSE

By

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KEY TO SYMBOLS

ABD	Abdomen
BW	Body weight
Cdyn	Dynamic lung compliance
C_L	Quasi-static lung compliance
C_W	Quasi-static chest wall compliance
C_{RS}	Quasi-static respiratory system compliance
EEV	End-expiratory lung volume
ERV	Expiratory reserve volume
EMG	Electromyogram
Eabd	Abdominal muscle electromyogram
Edi	Diaphragm electromyogram
Eint	Intercostal muscle electromyogram
f	Frequency of breathing
FRC	Functional residual capacity
IC	Inspiratory capacity
LW	Lung weight
OCW	Resting volume of the chest wall
Pao	Airway pressure, measured at the mouth
Pbs	Body surface pressure
Pes	Esophageal pressure
ΔPesmax	Maximum change in esophageal pressure during inspiration

Pdi	Transdiaphragmatic pressure
ΔPdi	Net change in transdiaphragmatic pressure
Pga	Gastric pressure
ΔPgamaxI	Net change in gastric pressure during inspiration
ΔPgamaxE	Net change in gastric pressure during expiration
Prs	Transrespiratory pressure
Ptp	Transpulmonary pressure
PtpFRC	Elastic recoil pressure of the lungs at FRC
P-V	Pressure-volume
RC	Resistance X compliance, measure of time constant
RC	Rib cage
RIP	Respiratory inductance plethysmography
Rpul	Total pulmonary resistance
RV	Residual volume
SA	Surface area
T_I	Inspiratory time, mechanical
T_E	Expiratory time, mechanical
T_{Ipeak1}	Time to first peak of inspiratory flow
T_{Epeak1}	Time to first peak of expiratory flow
T_{Idip}	Time to low point in inspiratory flow
T_{Edip}	Time to low point in expiratory flow
T_{Ipeak2}	Time to second peak of inspiratory flow
T_{Epeak2}	Time to second peak of expiratory flow
T_{TOT}	Total breath duration

T_I/T_{TOT}	Respiratory duty cycle
TLC	Total lung capacity
$\dot{V}$	Airflow
$\dot{V}_A$	Alveolar ventilation
$\dot{V}_E$	Minute ventilation
$\dot{V}_{Ipeak1}$	First peak of inspiratory flow
$\dot{V}_{Epeak1}$	First peak of expiratory flow
$\dot{V}_{Idip}$	Low point of inspiratory flow
$\dot{V}_{Edip}$	Low point of expiratory flow
$\dot{V}_{Ipeak2}$	Second peak of inspiratory flow
$\dot{V}_{Epeak2}$	Second peak of expiratory flow
$\dot{V}$meanI	Average inspiratory flow, from digitized flow tracing
$\dot{V}$meanE	Average expiratory flow, from digitized flow flow tracing
$\dot{V}_{O_2}$	Oxygen consumption
Vrx	Relaxation volume of the respiratory system
Vt	Tidal volume
Vt/T_I	Mean inspiratory flow
Vt/T_{TOT}X 60	Instantaneous minute ventilation

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DEVELOPMENTAL CHANGES IN RESPIRATORY MECHANICS AND BREATHING STRATEGY IN THE GROWING HORSE

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The respiratory muscle activation pattern responsible for the polyphasic pattern of breathing of the adult horse at rest was determined, to test the hypothesis that end-expiratory lung volume (EEV) is less than the relaxation volume of the respiratory system (Vrx). To further define the mechanisms responsible for transition from the neonatal to adult equine breathing pattern, the changes in breathing strategy and respiratory mechanics associated with maturation were investigated in the foal during the first year of life.

In the adult horse, electromyographic and pressure data indicated that both inspiration and expiration were composed of an active and passive component. This resulted in a breathing strategy in which the expiratory muscles shared the work of breathing with the inspiratory muscles and allowed the horse to breathe around, rather than from Vrx. The typical neonatal foal breathing strategy was characterized by a monophasic inspiratory and expiratory flow pattern. Both inspiration and expiration were active, with phasic abdominal muscle activity detectable through most of expiration. No evidence was found to support the hypothesis that the standing neonatal foal actively maintains EEV above Vrx, as reported in other neonatal species. The transition to the adult pattern of breathing involved an increasing delay in activation of first expiratory, and then inspiratory muscle groups, and was essentially complete by one year of age.

Quasi-static pressure-volume curves were generated in a group of anesthetized foals at specified intervals during the first year of life. In the neonatal foal, lung volumes normalized to body weight were similar to those reported in other neonatal species, while normalized chest wall compliance was lower. With maturation, normalized chest wall compliance and the unstressed volume of the chest wall decreased, while other parameters, including normalized lung compliance and Vrx, showed little change. The growth of the respiratory system was dysanaptic, with increases in lung volume lagging increases in overall body size.

It was concluded that, while the respiratory system of a relatively mature neonate such as the foal shares with

other species certain neonatal characteristics, the transition to adulthood differs in pattern and time frame between species.

GENERAL INTRODUCTION

The respiratory system of the horse has been of considerable interest to man for many years. Since ancient times, a number of authors have described the clinical and pathological characteristics of equine respiratory diseases and have speculated as to their etiology. Aristotle, in 333 B.C., was the first to describe a respiratory disease in the horse characterized by a "drawing in the flank" (Gillespie and Tyler, 1969), and several early authors, including Floyer (1698), Gibson in 1751 (cited in Smith, 1924), and Percivall (1853), further documented this syndrome of pulmonary emphysema or "broken wind" in the horse. Stommer (1887) was the first to note the similarities between emphysema in the horse and man. Malkmus (1913) recognized that a variety of pathological lesions could result in the same clinical signs of respiratory disease, and Kountz and Alexander (1934) further defined the pathological process in the horse as well as in other species. The majority of this attention stemmed from the fact that chronic respiratory disease was a major cause of disability in the working horse and resulted in serious financial losses to those who owned horses.

Reports concerning the normal respiratory system of the horse are much less common. It was only recognized around the turn of the century (Gmelin, 1910) that the normal horse at rest utilized a distinctive breathing pattern characterized by a double peak of flow and pressure during expiration. The author attributed this finding to a passive and active component of abdominal movements. McCutcheon (1951) reported that inspiration as well as expiration was typically polyphasic and suggested that variations in airway resistance during the breathing cycle were responsible for generation of this pattern. Amoroso et al. (1963), in a study of the airflow pattern of a number of different adult animal species, reported that the equine species appeared to be the only animals that utilized a polyphasic breathing pattern. The authors also found of considerable interest that while the adult equine consistently displayed this distinctive airflow pattern, the two immature (5 and 6 months of age) horses studied displayed only a monophasic pattern more closely resembling the pattern observed in the other adult animal species. They assumed therefore that a transition to an adult airflow pattern occurred sometime later than 6 months of age, but they did not know whether it occurred as a normal physiological development or as the result of some pathological process peculiar to the equine species.

Since that time, although interest has continued in certain aspects of pulmonary function in both the normal and diseased adult horse, no studies could be located which further investigated the developmental aspects of breathing in the growing foal. In addition to the insight into developmental respiratory physiology that such studies could provide, knowledge of normal pulmonary function in the growing foal is crucial for understanding the effect of disease states on the respiratory system. As respiratory disease remains an extremely important cause of morbidity and mortality in the foal, it was found surprising that so little information had been reported regarding either normal or abnormal pulmonary function in any age foal.

In this study of the changes in breathing strategy associated with growth in the horse during the first year of life, four hypotheses were tested. Throughout this manuscript, the term breathing strategy is used to refer to the specific pattern of coordinated activity of pump and upper airway muscles adopted by an individual to bring about a tidal breath.

1. The polyphasic airflow pattern previously reported in the adult horse at rest is due to a respiratory muscle activation pattern that results in the generation of a strategy to breathe around, rather than from, the relaxation volume of the respiratory system.

2. The mechanical characteristics of the respiratory system of the neonatal foal are similar to those of other neonatal species, and the type of breathing pattern utilized by the foal is influenced by these properties. More

specifically, it is hypothesized that the neonatal foal does not display the adult breathing pattern, but rather uses a different strategy to breathe above or from the relaxation volume of the respiratory system.

3. The neonatal pattern of breathing matures to that of the adult within the first year of life.

4. The change in breathing pattern with development in the horse is explained by a decrease in chest wall compliance.

In order to test these hypotheses, several studies were performed. In the first study the respiratory muscle activation pattern and resulting pressures were measured concurrently with airflow to identify the mechanism responsible for the polyphasic flow pattern in the adult horse. In another series of studies, the same parameters were measured in a group of neonatal foals in order to determine the typical breathing patterns utilized by this species of neonate. Similar studies were completed at a total of 10 different age groups during the first year of life to document any changes in ventilatory and/or breathing pattern associated with maturation. In the same group of foals, and at approximately the same ages, the static mechanical properties of the lungs and chest wall were also determined. The ages at which substantial changes were noted in breathing pattern were compared with the time frame in which certain mechanical properties, in particular, of the chest wall, were changing in order to identify any association between the two.

In addition to addressing the specific questions concerning maturation of breathing strategy in the horse, it was hoped that the information acquired would be useful from a comparative physiological standpoint as well. Almost all previous studies of neonatal breathing strategy and respiratory mechanics have been performed in species that are smaller and less mature at birth than the human infant. The foal is a much larger and more precocious neonate. Investigations conducted in this species should therefore provide information on the validity of extrapolation of the current concepts of neonatal breathing strategy and respiratory mechanics to neonates of larger body size. In addition, complete, sequential studies of the maturation of the respiratory system during growth have rarely been performed in any species, including the human, and information generated in the present studies should add to the body of knowledge in this area. Finally, it has been suggested (Smith and Loring, in press) that investigations of variations in chest wall mechanical characteristics across various mammalian species should be performed to provide important functional insight on the design of the chest wall, particularly in relation to body size, posture, and constraints imposed by gravity. By these criteria, as the horse undergoes a rapid increase in size during maturation, from approximately 45 kg at birth to 450 kg as an adult, this species should be an ideal species in which to study chest wall mechanics.

CHAPTER I
BREATHING STRATEGY OF THE ADULT HORSE AT REST

Introduction

It has been recognized for many years that the adult horse at rest utilizes a breathing strategy distinct from most other domesticated and laboratory animals. Gmelin (1910) reported that expiration in the adult horse was accompanied by a double peak of flow and pressure. McCutcheon (1951) documented that inspiration could also have a biphasic character. Furthermore, in a study of breathing strategies of several domesticated animal species, including the awake dog, sheep, goat, cow, pig, donkey, mule, horse, chicken, and duck (Amoroso et al., 1963), the Equidae were the only animals observed to breathe with both a biphasic inspiratory and expiratory flow pattern. It was not established, however, that all of the animals were relaxed and breathing quietly during those studies. Gillespie et al. (1966), in a study of the respiratory system of normal and diseased horses, confirmed the polyphasic breathing pattern of the normal adult horse at rest but added that this characteristic flow pattern was abandoned during excitation, exercise, or in pathological conditions such as emphysema or chronic bronchitis.

Few studies have explored the mechanism underlying the polyphasic flow pattern. Robinson et al. (1975) suggested that this unique flow pattern could be generated by fluctuations in airway resistance, asynchronous movement of the ribs and abdomen, or by a combination of active and passive breathing. They explored the first possibility by measurement of the resistance of different segments of the respiratory tract. No substantial change was found in upper airway resistance during inspiration or expiration that could account for the marked changes in flow rates (Robinson et al., 1975). Several investigators (Derksen and Robinson, 1980; Gillespie et al., 1966) have observed that the second phase of expiration is accompanied by contraction of the abdominal musculature. In addition, a midexpiratory cessation of air flow has been reported in sedated, tracheostomized ponies (Derksen and Robinson, 1980). The authors speculated that the lung volume during this pause represented the relaxation volume (Vrx) of the respiratory system, defined as the equilibrium position where the tendency of the lungs to recoil inward is equal to the tendency of the passive chest wall to recoil outward. Any decrease in volume from this mechanical equilibrium position would have to be accomplished by activation of the expiratory muscles. Based on this circumstantial evidence, it has been suggested that the horse may breathe around, rather than from Vrx, as is assumed to occur in most other mammals (Derksen and Robinson, 1980). There have been no studies, however, that have documented the sequence of respiratory muscle activation associated with the adult horse's breathing pattern.

In the present investigation, I have extended the previously mentioned observations to examine the sequence of respiratory muscle activation, the pressures generated by their action, and the accompanying airflow and volume excursions during quiet tidal breathing. The purpose of this study was to test the hypothesis that the normal adult horse at rest breathes around the relaxation volume of the respiratory system.

Materials and Methods

Nine adult horses between 2-13 years of age (6.2 ± 3.8 yrs, mean ± SD) and weighing 432-555 kg (474 ± 44 kg) were used for the breathing studies. Eight were non-pregnant females and one was a castrated male; breeds included seven grade individuals (Quarterhorse and Thoroughbred type), one American Saddlebred and one Arabian. All of the animals were maintained on pasture prior to the studies and on physical examination were free of clinical signs of respiratory disease. For the studies, the horses were restrained in a set of stocks to which they had previously been accustomed. Five of the nine horses (#1, 2, 4, 5, 9) required tranquilization with a low dose of xylazine (Rompun, Haver-Lockhart; 0.15-0.25 mg/kg intravenously) to facilitate instrumentation. Measurements, however, were recorded at least 45 minutes after the drug was given, when the animals appeared bright, alert and free of any signs of tranquilization. The respiratory parameters measured in the sedated horses were compared to those of the non-sedated individuals to detect any persisting influence of xylazine on the breathing pattern. In three horses, it was necessary to repeat measurements on two or three separate occasions in order to acquire both electromyograms (EMG) and pressure data.

For measurement of airflow ($\dot{V}$), tidal volume (Vt), and airway pressure (Pao), a fiberglass facemask holding two Fleisch No. 4 pneumotachographs was utilized. A band of rubber innertube material cemented to the fiberglass was secured to the head of the horse with electrical tape to form an airtight seal (Fig. 1-1). The mask was positioned so that the nostrils were unobstructed and in a direct line with the pneumotachographs. The two pneumotachographs were used in parallel and the combined pressure drop across them, proportional to airflow, was measured using a ± 5 cm H_20 differential pressure transducer (Validyne model MP-45). The flow signal was electronically integrated to yield volume (Validyne model FV 156 integrator). The system was calibrated over the experimental ranges of tidal volume and airflow by forcing known volumes and airflows through the pneumotachographs, generated and measured, respectively, by a calibrated super-syringe and a rheostat controlled vaccuum cleaner system and flow rotameter. The Pao was measured with another ± 2 cm H_20 differential pressure transducer from the proximal port of the pneumotachographs.

Esophageal (Pes) and gastric (Pga) pressures were recorded with 7-8 cm long, thin walled balloons (fingers cut from a surgical glove) sealed over the end of Teflon PFA tubing (Cole Palmer Instrument Co.; internal diameter 2 mm, and 275 cm long) that had a number of perforations in the tubing underlying the balloon. Each catheter was connected via a 3-way stopcock to the positive side of a ± 50 cm H_2O differential pressure transducer, with the negative side left open to the atmosphere. Both Pga and Pes balloons were routinely filled with 2 ml of air during the studies, as pressure-volume curves of the balloon-catheter systems indicated that this amount was within their appropriate volume range. The frequency response of the balloon-catheter system was tested using the method of Jackson and Vinegar (1979). A flat response in amplitude was observed up to 15 Hz; at a frequency of 5 Hz there was a 20 degree phase lag. This response was considered more than adequate for measurement of respiratory parameters in quietly breathing horses. All pressure transducers were calibrated using a water manometer system before and at the end of each experiment.

Electromyograms (EMGs) were recorded from the intercostal and abdominal musculature and from the diaphragm. For the measurement of intercostal (Eint) and abdominal (Eabd) EMGs, bipolar, fine stainless steel wire electrodes (28 AWG) were placed intramuscularly using a technique similar to that described by Basmajian and Stecko (1962). Prior to placement, the proximal and distal 2 mm of the wires were stripped of insulation, and the wires were then threaded through 16 gauge needles so that about 2 mm protruded from the tip of the needle. These ends were then bent over to lie flush with the shaft of the needle to facilitate passage through the skin. After a nick was made in the skin with a scalpel blade, the sterilized needle was passed into the muscle, and then gently withdrawn, leaving the wires in place. The electrode wires were then connected by fine clips to a cable connected to a differential amplifier (Tektronix model AM502).

For recording Eint, identical wire electrodes were placed in the right 11th intercostal space, at a depth of approximately 2 cm. Placement of the wires was probably within the external intercostal muscles as the EMG recordings showed inspiratory burst activity in all studies. Abdominal muscle wire electrodes were placed in the ventral flank area, presumably in the internal abdominal oblique muscle (Fig. 1-2).

The EMG signal from the diaphragm (Edi) was measured using paired silver electrodes built into a hollow plastic catheter (internal diameter 2 mm, length 3.5 m) which was placed in the lower esophagus close to the stomach, as previously described in humans (Agostoni et al., 1960). For use in the adult horse, an inter-electrode distance of 3.75 cm was used (Fig. 1-3A). A balloon attached to the end of the catheter and located in the stomach was inflated with 30 cc of air in order to anchor the tubing so that the electrode gave a useful Edi signal during breathing excursions (Fig. 1-3B). All EMG signals were bandpass filtered between 100 and 3000 Hz with attenuation slopes of 3dB/octave by the differential amplifiers.

All three balloon-catheter systems were passed into the horse's stomach in a well-lubricated adult horse nasogastric tube. The balloon portions of all catheters were advanced out of the tube, the balloons were inflated, and the nasogastric tube was retracted, leaving the catheters in place. The esophageal balloon was repositioned into the lower esophagus by observation of a change to a negative pressure deflection during inspiration on a storage oscilloscope (Tektronix model 5113).

All signals were recorded on an FM tape recorder (Hewlett-Packard model 3968A) while the horses were breathing quietly. For analysis, taped data were replayed onto an 8-channel pen writer (Gould model 28007) or a storage oscilloscope. At least one set of 10 consecutive breaths was analyzed per experiment, and in some animals data from several sets of 5 to 10 consecutive breaths were analyzed and averaged. As both inspiratory and expiratory flow rates were biphasic, the two peaks of flow ($\dot{V}$peak1 and $\dot{V}$peak2) and the intervening low point in flow ($\dot{V}$dip) were measured for both inspiration and expiration. In addition, $\dot{V}$ and Vt signals were displayed on an X-Y storage oscilloscope and the flow-volume loops for individual breaths were photographed with a Polaroid camera.

Mechanical inspiratory (T_I) and expiratory (T_E) times were determined from the zero crossover points on the flow tracing. The Vt was measured from the volume tracing. The ratio of T_I:T_E, total breath duration (T_{TOT}), instantaneous breathing frequency ($1/T_{TOT}$ X 60), and minute ventilation ($1/T_{TOT}$ X 60 X Vt) were calculated breath-by-breath and averaged. In addition, the times within each inspiration and expiration when $\dot{V}$peak1, $\dot{V}$peak2, and $\dot{V}$dip occurred were recorded. The time intervals between onset of inspiratory flow and onset of both Edi and Eint were recorded for each breath and averaged. The same comparison was made between onset of expiratory flow and Eabd. These intervals were expressed in both seconds and as a percent of T_I or T_E. In selected breaths, the raw Eabd or Edi signal was electrically added to the flow signal and plotted against volume on an X-Y storage oscilloscope.

For calculation of dynamic compliance (Cdyn), Vt was divided by the difference in esophageal pressure at the two points of zero airflow. Inspiratory and expiratory pulmonary resistance (Rpul) was calculated at 25, 50, and 75% of Vt using a modification (Robinson et al., 1975) of the technique first described by Neergaard and Wirz (1927) which was adapted for the equine by Gillespie et al. (1966). The 3 values obtained for inspiration and expiration were averaged to obtain a mean inspiratory and expiratory Rpul. The maximum change in Pes between expiration and inspiration (Δ Pesmax) was measured. The maximal change in Pga (ΔPgamax) during both inspiration and expiration was also measured. A continuous record of transdiaphragmatic pressure (Pdi) was obtained by electrical subtraction of Pga from Pes. The net change in Pdi (ΔPdi) during both inspiration and expiration was measured and the ratio between the two was calculated. Finally, the time interval between onset of inspiratory flow and a decrease or change in downward slope of Pdi was measured.

In 3 of the horses studied, respiratory inductance plethysmography (RIP) was utilized to rule out the possibility that the application of a facemask was in some way altering the normal breathing of the horse. Large animal RIP respibands were applied to the rib cage (RC) and abdomen (ABD). The leads from each band were attached to a customized large animal oscillator unit, and the outputs from both bands were equally gained at the demodulator unit (Ambulatory Monitoring, Inc). Both signals were low-pass filtered at 5 Hz (Rockland model 452). The sum of the RC and ABD displacements (a signal proportional to Vt) was plotted against the differentiated sum (a signal proportional to airflow) on an X-Y oscilloscope. The similarity of the RIP generated loops to those simultaneously measured at the mouth by the pneumotach system was evaluated. In addition, the loops generated by the RIP system while the horses had no facemask were compared to those acquired with the pneumotach system in place.

Results

Table 1-1 shows the individual and mean data on age and ventilatory parameters of the nine horses studied. All animals displayed a biphasic airflow pattern during both inspiration and expiration. In five of the nine animals, the second peak of inspiratory flow ($\dot{V}_{Ipeak2}$) was greater than the first ($\dot{V}_{Ipeak1}$), while during expiration, in all but one horse, the first peak of flow ($\dot{V}_{Epeak1}$) was higher than the second ($\dot{V}_{Epeak2}$). Table 1-2 lists the mechanical timing parameters and their relation to the onset of the EMG signals. A composite breath, constructed by plotting the mean values of airflow and timing parameters of all nine horses, is shown in Figure 1-4 and in the schematic diagragm in Appendix A. The average times at $\dot{V}_{Ipeak1}$, $\dot{V}_{Idip}$, and $\dot{V}_{Ipeak\ 2}$ of flow were 0.41 ± 0.14, 1.05 ± 0.28, and 1.99 ± 0.44 seconds (mean ± SD), or 15.7%, 43.2%, and 76.5% of T_I, respectively. For expiration, similar times referenced to the onset of T_E occurred at 0.36 ± 0.18, 1.45 ± 0.69, and 2.86 ± 1.08 seconds, or at 10.8%, 39%, and 79% of T_E.

Abdominal, intercostal and diaphragm EMG activities were consistently recorded from all horses studied. In all three muscle groups, the average onset of EMG activity lagged the mechanical onset of inspiration or expiration, establishing an active and passive phase during both inspiration and expiration (Table 1-2). For inspiration, Edi lagged the mechanical onset of inspiratory flow by an average of 0.37 seconds, or 17.1% of the average T_I, and

Table 1-1. Ventilatory parameters in the normal adult horse at rest.

Horse	Age (years)	V_t (L)	$\dot{V}_{Ipeak1}$	$\dot{V}_{Idip}$ (L/min)	$\dot{V}_{Ipeak2}$	$\dot{V}_{Epeak1}$	$\dot{V}_{Edip}$ (L/min)	$\dot{V}_{Epeak2}$	$\dot{V}_E$ (L/min)	f
1	3	6.8	120.5	69.5	130.5	100.5	59.5	96.0	54.2	8
2A	4	5.8	184.8	155.3	255.8	284.7	149.3	203.0	88.1	15.3
B		7.3	290.0	152.7	281.7	299.6	69.2	295.1	86.7	11.9
3	8	6.4	312.6	177.8	338.1	437.1	215.9	236.4	122.0	19.0
4	12	8.1	217.1	134.3	251.6	341.6	58.9	118.5	66.5	8.2
5	3	8.5	135.9	106.6	129.6	139.7	35.9	74.7	52.3	6.2
6A	2	5.7	190.3	83.3	177.4	151.7	50.0	172.7	56.5	10.0
B		5.4	260.8	152.4	249.6	343.8	245.6	251.4	111.3	20.5
C		5.8	211.6	116.7	205.0	208.4	158.4	218.3	91.5	15.7
7	4	4.5	208.1	91.9	148.1	219.4	189.4	206.3	72.0	16.0
8	9	8.1	173.4	88.0	209.3	212.0	33.3	124.0	67.6	8.4

Table 1-1. continued

Horse	Age (years)	V_t (L)	$\dot{V}_{Ipeak1}$	$\dot{V}_{Idip}$ (L/min)	$\dot{V}_{Ipeak2}$	$\dot{V}_{Epeak1}$	$\dot{V}_{Edip}$ (L/min)	$\dot{V}_{Epeak2}$	$\dot{V}_E$ (L/min)	f
9A	11	6.3	282.2	132.0	288.2	330.1	39.6	193.9	62.3	10.0
B		4.8	310.6	162.4	252.4	302.7	170.3	213.6	102.4	21.3
$\overline{X}$	6.2	6.7	213.6	120.8	217.4	254.8	106.5	169.2	76.8	12.3
±SD	±3.8	±1.3	±64.9	±35.3	±71.9	±104.0	±66.8	±65.6	±21.2	±4.6

V_t = tidal volume, $\dot{V}_{Ipeak1}$, $\dot{V}_{Idip}$, $\dot{V}_{Ipeak2}$ refer to the first peak, low point, and second peak of inspiratory flow; $\dot{V}_{Epeak1}$, $\dot{V}_{Edip}$, $\dot{V}_{Epeak2}$ refer to the same points of expiratory flow. $\dot{V}_E$ = minute ventilation. A, B, C refer to different study days for the same animal; numbers from each day are averaged and an average value for each horse is used for overall calculations. f = breaths per minute.

Table 1-2. Timing parameters in the normal adult horse at rest.

Horse	T_I	Difference:* Onset of T_I vs $T_{I(Edi)}$		Difference:* Onset of T_I vs $T_{I(Eint)}$		T_E	Difference:* Onset of T_E vs $T_{E(Eabd)}$		T_{TOT}	$T_1:T_E$
	(S)	(S)	(% T_I)	(S)	(% T_I)	(S)	(S)	(% T_E)	(S)	
1	3.63	NR	NR	NR	NR	3.85	NR	NR	7.48	0.94
2A	1.79	-0.55	-30.6	-0.08	-4.5	2.12	-0.46	-21.5	3.91	0.87
B	2.28	NR	NR	-0.24	-10.4	2.78	-1.04	-37.4	5.06	0.82
3	1.53	+0.03	+1.8	NR	NR	1.63	-0.75	-46.0	3.20	0.92
4	3.19	NR	NR	-0.24	-7.4	5.04	-1.13	-22.4	8.20	0.63
5	3.09	NR	NR	-0.22	-7.2	6.61	-3.11	-47.1	9.70	0.47
6A	2.67	-0.63	-23.4	NR	NR	3.40	-2.00	-59.4	6.00	0.79
B	1.53	-0.05	-3.3	+.003	+0.2	1.40	NR	NR	2.90	1.10
C	1.89	-0.20	-10.6	-0.34	-18.0	1.90	-0.23	-11.8	3.80	0.97
7	2.15	-0.78	-36.1	NR	NR	1.63	-0.36	-21.9	3.80	1.32
8	2.97	-0.52	-17.6	NR	NR	4.19	-1.80	-41.7	7.20	0.71

Table 1-2. continued

Horse	T_I	Difference:* Onset of T_I vs $T_{I(Edi)}$		Difference:* Onset of T_I vs $T_{I(Eint)}$		T_E	Difference:* Onset of T_E vs $T_{E(Eabd)}$		T_{TOT}	$T_1:T_E$
	(S)	(S)	(% T_I)	(S)	(% T_I)	(S)	(S)	(% T_E)	(S)	
9A	2.13	NR	NR	-0.59	-27.8	3.92	NR	NR	6.10	0.54
B	1.31	-0.1	-7.5	NR	NR	1.50	-0.08	-5.5	2.80	0.87
$\overline{X}$	2.48	-0.37	-17.1	-0.27	-11.8	3.37	-1.14	-31.2	5.86	0.83
$\pm$SD	$\pm$.74	$\pm$.30	$\pm$14.3	$\pm$.18	$\pm$9.0	$\pm$1.69	$\pm$.95	$\pm$14.3	$\pm$2.31	$\pm$.24

*Minus sign denotes that onset of neural time lags mechanical event (beginning of inspiratory or expiratory flow). Plus sign denotes that onset of neural time precedes mechanical event.

T_I = mechanical inspiratory time, T_E = mechanical expiratory time, T_{TOT} = time for combined mechanical $T_I + T_E$. NR = not recorded.

A, B, C refer to different study days for the same animal; numbers from each day are averaged and an average value for each horse is used for overall calculations.

Eint lagged by 0.27 seconds or 11.8% of T_I. During expiration, Eabd lagged the mechanical onset of expiratory flow by an average of 1.14 seconds or 31.2% of the average T_E.

The Edi signal persisted into expiration (Figure 1-5A) in all but one horse (#7) and the Eabd signal persisted into inspiration (Figure 1-6A) in four of the nine animals. Representative flow-volume loops of two horses are presented in Figures 1-5B,C and 1-6B,C. With the Edi or Eabd signals superimposed on the flow tracings, creating "paintbrush flow-volume loops," the active and passive components of both inspiration and expiration are easily recognized. For example, in Fig. 1-5B, the majority of the Edi signal coincides with the second phase of inspiratory flow, and in Fig. 1-5C, Eabd is associated with only the second phase of expiration. The segments of the loops devoid of EMG signals are considered to be the passive components of inspiration and expiration.

There was considerable variation, most notably between animals, but also within some individuals, in both the biphasic character of the flow-volume loops and in the phase lag between airflow and EMG activities (Figs. 1-5 and 1-6). There were no differences noted in these parameters between the 5 horses which received xylazine and the four which did not. Onset of Eint and Edi did slightly precede the onset of inspiratory flow in one horse (#3), but in all horses the major burst of diaphragmatic EMG was observed during the second phase of inspiratory flow. Likewise, there was considerable variation in time of onset of Eabd. These variations in muscle activation pattern were found to result in different configurations of flow-volume loops. In some animals, airflow decreased to near zero at mid-inspiration or mid-expiration before respiratory muscle activity was detectable, exaggerating the biphasic configuration of the flow-volume loop. In others, EMG activity was noted during early inspiration or expiration, making the passive component of the phase relatively short and effectively smoothing out the biphasic configuration of the loop.

Representative tracings of Pes, Pga, Pdi, and $\dot{V}$ are displayed in Fig. 1-7, and average values for all horses are given in Table 1-3. Two peaks of Pga were observed during each breathing cycle in all horses studied. The inspiratory peak (pt. A, Fig. 1-7) coincided with or occurred shortly before the zero flow point between inspiration and expiration. The expiratory peak of Pga (pt. B, Figure 1-7) was observed during the second phase of expiration, shortly before the mechanical transition between expiration and inspiration. The low point in Pga during expiration was observed at or shortly before $\dot{V}_{Edip}$ and the low point in Pga during inspiration was observed an average of 0.28 ± 0.21 seconds before $\dot{V}_{Idip}$. In all horses, the average change in Pga associated with expiration was greater than that associated with inspiration (Table 1-3). The lowest (most negative) value of Pes corresponded to the second phase of inspiratory flow and the highest (least negative) value was

Table 1-3. Pressure changes during quiet breathing in the adult horse.

Horse	V_T (L)	f	ΔP_{esmax} (cmH_2O)	ΔP_{gaI} (cmH_2O)	ΔP_{gaE} (cmH_2O)	ΔP_{diI} (cmH_2O)	ΔP_{diE} (cmH_2O)	$\Delta P_{diE}/\Delta P_{diI}$	$T_I\Delta P_{di}$ (S)
1	6.8	8.0	9.80	2.13	3.89	-6.56	NC	0	-1.14
2	7.3	12.0	5.06	1.85	5.50	-3.13	-3.45	1.10	-1.10
3	6.4	19.0	8.19	1.25	2.21	-7.82	NC	0	0.0
4	8.1	8.2	8.30	3.00	4.62	-4.45	-1.25	0.28	-1.14
5	8.5	6.2	5.39	4.00	4.50	-5.65	NC	0	-0.74
6	5.7	10.0	7.44	.88	6.83	-3.25	-4.30	1.32	-1.50
8	8.1	8.4	5.50	2.62	3.15	-4.63	-1.21	0.41	-1.11
9	6.3	9.9	5.94	3.24	4.65	-6.16	-1.85	0.30	-0.72
$\overline{X}$	7.2	10.2	6.95	2.37	4.42	-4.83	-2.41		-0.931
±SD	±1.1	±3.9	±1.73	±1.05	±1.41	±1.35	±1.40		±.450

ΔP_{esmax} = maximal change in P_{es} from end-expiration to peak value during inspiration. ΔP_{ga} + ΔP_{di} = maximal increase (+) or decrease (-) in gastric and transdiaphragmatic pressure during inspiration and expiration. $T_I\Delta P_{di}$ = time into inspiration when P_{di} begins to decrease or changes slope of descent. f = breaths per minute. NC = no change in P_{di} during expiration.

observed towards the end of the second phase of expiratory flow, and corresponded with the peak of Pga. The Pes tracing during expiration was often characterized by a pronounced peak (pt. C, Fig. 1-7) associated with $\dot{V}_{Epeak1}$; a similar, but less pronounced rise (pt.D, Fig 1-7) was sometimes associated with $\dot{V}_{Ipeak1}$ as well. The Pdi reached a minimum value (representing the maximal generated pressure) during the second phase of inspiratory flow in all horses. In five horses, Pdi consistently decreased through the second phase of expiration and in horses #2 and #6, this change was greater than that observed during inspiration (Table 1-3). In seven horses, a downward deflection or an increased rate of decline of Pdi (pt. E, Fig. 1-7) lagged the onset of inspiratory flow by an average of 0.93 ± 0.45 seconds and was more closely associated with $\dot{V}_{Idip}$ (preceding it by an average of 0.22 ± 0.11 sec).

Dynamic compliance averaged 2.65 ± 1.51 L/cmH_2O. Mean inspiratory pulmonary resistance was 0.0134 ± 0.008 cmH_2O/L/min. and mean expiratory pulmonary resistance was 0.0132 ± 0.007 cmH_2O/L/min.

The RIP-generated flow-volume loops acquired with the facemask in place were not appreciably different than those obtained when the facemask was absent (Fig. 1-8).

Discussion

Analysis of the pattern of respiratory muscle activation compared to changes in airflow showed that detectable inspiratory muscle EMG activity lagged the onset of inspiratory flow in all but one horse, and that the onset of expiratory (abdominal) muscle EMG activity lagged the onset of expiratory flow in all horses studied. Thus, the classic descriptions of inspiration as a primarily active, and expiration as a primarily passive process are not appropriate for the adult horse. Rather, it is evident from the EMG data that there was a passive and active phase to both inspiration and expiration. The first part of expiration was primarily passive, as in man, with deflation toward Vrx, but subsequent activation of abdominal muscles was responsible for a second phase of expiration: active deflation to below Vrx. From end-expiratory volume, passive inflation was possible back towards Vrx, utilizing the energy stored during the active phase of expiration. This was followed by a second phase of inspiration: active inflation to above Vrx, brought about by both diaphragmatic and intercostal muscle activation. In this way the adult horse is able to breathe around, rather than from Vrx, as is clearly seen by examination of the paintbrush flow-volume loops (Figs. 1-5B,C and 1-6B,C). Although this basic pattern held for all animals studied, the relative proportions of the active and passive components of both inspiration and expiration varied.

Pressure changes measured during the breathing cycle were also supportive of a strategy of breathing around Vrx. Analogous to quiet expiration in man, the decreasing Pga and increasing Pes observed during the first part of expiration (Fig. 1-7) were compatible with a passive process. However, with the activation of abdominal muscles during the second, active phase of expiration, an increase in Pga was always observed, along with a concurrent smaller increase in Pes as pressure generated in the abdomen was passively transmitted through the diaphragm. After reaching a maximum near or at end-expiration (Fig. 1-7, pt. B), both Pes and Pga continued to decrease through the first part of inspiration. This decrease in Pga is compatible with, but not strictly limited to, a primarily passive inflation toward Vrx. With the subsequent onset of inspiratory muscle activity, Pes continued to decrease to a minimum value with continued expansion of the chest wall, and gastric pressure rose, as a result of activation and caudal displacement of the diaphragm. As in man, Pga and Pes reached a maximum (Fig. 1-7, pt. A) and minimum, respectively, at the time of maximal diaphragmatic activity. The maximum change in Pdi was also generated during the last part of inspiration as a result of diaphragmatic contraction, analogous to inspiration in most other mammals. In five horses, an obvious decline in Pdi was observed in many of the breaths during the second phase of expiration and the first phase of inspiration (Fig. 1-7, pt. E). In the absence of artifacts associated with the pressure measurements, this decrease in Pdi without associated diaphragmatic contraction suggests that the diaphragm was being passively stretched as a result of abdominal muscle activation. This would be expected because as the abdominal wall is displaced inward at low lung volumes (less than Vrx), the diaphragm passively resists stretching, resulting in a greater increase in pressure on the abdominal than on the pleural side and a more negative Pdi (Mead, 1976). The peak of Pes consistently associated with $\dot{V}_{Epeak1}$ (Fig 1-7, pt. C) appeared to result from dynamic resistive losses during the period when the flow rate was high. The similar, but less obvious peak observed during the first phase of inspiration (Fig. 1-7, pt. D) probably resulted from the same mechanism. This phenomenon may have been less pronounced during inspiration because the peak flow rates during the first part of inspiration were lower than those recorded during the first part of expiration. Although the absolute values of Pga and Pes varied between horses, and thus affected the Pdi tracing, the pattern of change was consistent in all horses. As has been described in humans (Mead, 1976), Pga was generally found to be a fixed amount more positive than Pes, due to gastric tone. Thus, Pdi as calculated was less than zero throughout the breathing cycle.

Some degree of persistent (post-inspiratory) inspiratory muscle activity during the first phase of expiration was commonly observed. This was assumed to serve the same function in the horse as in other species with primarily passive expirations, that is, to prevent an abrupt transition between inspiration and expiration by braking potentially high expiratory flow rates (Murphy et al., 1959; Petit et al., 1960). In five of the horses studied, persistent expiratory muscle activity was observed during the first part of inspiration as well. This phenomenon should be advantageous to an animal when passively inflating from end-expiration toward Vrx. In this circumstance, analogous to the situation during expiration, persistent expiratory muscle activity would be expected to retard an abrupt motion secondary to the elastic recoil forces of a stiff chest wall tending to expand in an outward direction.

The mean values for the ventilatory parameters of tidal volume, peak inspiratory and expiratory flow rate, breathing freqency, minute ventilation, dynamic lung compliance, and total pulmonary resistance in these horses were similar to those obtained in previous studies of normal adult horse pulmonary function (Amoroso et al., 1963; Gallivan, 1981; Gillespie and Tyler, 1969; Gillespie et al., 1966; Muylle and Oyaert, 1973; Willoughby and McDonell, 1979). There has been wide variation in reported values for Cdyn in normal awake horses, ranging from 0.8 (Dewes et al., 1974) to 6.13 L/cm H_20 (Gillespie and Tyler, 1969) but most of the values have fallen between 2.0 and 2.5 L/cm H_20 (Gallivan, 1981; Muylle and Oyaert, 1973; Willoughby and McDonell, 1979), which is similar to the mean value in the present study. Pulmonary resistance has been reported in several different ways, including peak (Gillespie and Tyler, 1969; Gillespie et al., 1966) and mean inspiratory and expiratory resistance

(Dewes et al., 1974), as well as resistance at 25, 50, and 75% of Vt during inspiration and expiration (Gallivan, 1981; Robinson et al., 1975). Mean resistance values of the present study are similar to the mean values that were reported by Dewes et al. (1974) but are somewhat higher than those reported in other studies (Gallivan, 1981; Gillespie and Tyler, 1969; Robinson et al., 1975).

An important concern in virtually any study that attempts to describe normal behavior in animals is that the methods utilized to acquire the desired data in some way may influence or alter the results. Most studies that have documented that the breathing pattern of the horse at rest is polyphasic in character have utilized a pneumotach system either applied to the face with a mask fitted over the muzzle (Amoroso et al., 1963; Gillespie et al., 1966) or to a tube placed in a tracheostomy opening (Derksen and Robinson, 1980). Examination of RIP generated flow-volume (sum-differentiated sum) loops generated both with and without a pneumotach-facemask system (Fig. 1-8) indicated that the facemask used in the present study did not artifactually determine the horse's breathing pattern. No appreciable difference in flow-volume loop configuration were observed under the two circumstances. In addition, in a previous study which compared the breathing mechanism of the horse and rat, McCutcheon (1951), using a nasal cannula instead of a facemask, observed a polyphasic airway pressure associated with quiet breathing in the horse. It was therefore concluded that the normal breathing pattern of the horse is not significantly affected by the presence of a facemask.

The results of this study do not constitute a complete description of the activation pattern of all the respiratory muscles of the adult horse during quiet breathing. The activities of only one expiratory muscle and two inspiratory muscles were measured. Three other large abdominal muscles (external abdominal oblique, transversus abdominis, and rectus abdominus) could and probably do contribute to the normal breathing strategy. It is possible that these muscle groups could be activated at different times during the breathing cycle, but this seems unlikely. In addition, my inability to obtain an expiratory signal from the intercostal muscles does not eliminate the possibility that they are phasically active during expiration. In fact, based on studies of breathing patterns in yearling horses (Chapter III) it is probable that expiratory intercostal activity is normally present in the adult horse at rest. Percutaneous placement of the wires properly into the desired intercostal muscle, however, can be a fairly tedious, trial and error procedure. The activity of other thoracic, primary or accessory respiratory muscles, such as the transversus thoracis, was not investigated in this study. Finally, a number of upper airway muscles may help to control airflow and thus act with the pump muscles to shape the overall respiratory pattern. This aspect was obviously not explored in the present study.

Another limitation of this study was a problem inherent in the use of wire EMG electrodes. The electrical activity of only a very small proportion of the total number of fibers in the large muscles was actually sampled, and generalizations were based on this small sample size. Diffferent regional activation patterns may exist, particularly in the case of the intercostal muscles, as they extend over a large portion of the body and probably play an important role in maintenance of posture, especially during movement and exercise. A similar criticism can be made of the type of surface Edi esophageal electrode that was utilized. The absence of a detectable signal does not necessarily indicate that the diaphragm was electrically silent. It is possible that the electrode was simply too far away from the signal to detect it. In addition, studies in sleeping lambs (Henderson-Smart et al., 1982) and anesthetized cats (Lunteren et al., 1985) suggest that under certain circumstances, the EMG activity of the costal portion of the diaphragm may differ from that of the crural part. An esophageal electrode would be expected to measure the activity of the crural diaphragm preferentially, but no data exist to suggest that the activation pattern is asynchronous in the horse. In addition, in the lamb study (Henderson-Smart et al., 1982) the major differences in electrical activity were related to post-inspiratory activity while the onset of activity appeared constant between the different parts of the diaphragm and also the intercostal muscles. Thus, a breathing strategy cannot be adequately described by analysis of the EMG pattern of the respiratory muscles alone. This is why I measured EMGs, generated pressures, and airflow to adequately describe the breathing pattern. For example, during expiration, the observed onset of abdominal muscle EMG activity shortly preceded both $\dot{V}_{Edip}$ and an increase in Pga, as would be expected during a transition from a passive to an active phase. During inspiration, the lag observed between onset of inspiratory airflow and EMG activation combined with a decreasing Pdi during expiration and a biphasic flow pattern are consistent with passive inflation from an end-expiratory lung volume lower than Vrx.

The physiological explanation for this adaptation in the breathing pattern in the equine species remains unclear. Although information on the subject is limited, it is probable that a number of quadruped mammals activate their abdominal muscles phasically during quiet breathing, at least in certain postures. Phasic abdominal EMG activity during expiration has been recorded in anesthetized cats (Chennells, 1957; Koehler and Bishop, 1979). The normal awake dog appears to use his abdomen both tonically and phasically in sitting and standing postures, but not in lateral recumbency (Banzett et al., 1980; Amis, T., personal communication). DeTroyer and Ninane (1985) have recorded phasic expiratory activity from the transversus thoracis muscle in spontaneously breathing, supine, anesthetized dogs. In no other species besides the equine, however, has a pronounced biphasic inspiratory and expiratory flow pattern been described, and to date there is little evidence that other species breathe substantially below Vrx. In dogs, phasic abdominal EMG activity is generally present through most of expiration, and neither inspiration nor expiration has a biphasic character. Recent work performed in anesthetized, supine dogs (DeTroyer and Ninane, 1985) does suggest that expiratory muscle activation does result in an end-expiratory lung volume which is somewhat less than Vrx. The applicability of this finding in the intact, awake dog still needs to be determined.

Even though the cow is of similar size to the horse, its frequency of breathing is considerably higher than that of the horse and its pattern of airflow during both inspiration and expiration is monophasic (Amoroso et al., 1963; Gallivan, 1981; Musewe et al., 1979). Gallivan (1981), in his study of the comparative aspects of the structure and function of the respiratory system of the horse and cow, did not find any significant differences in mechanical parameters between the two species that he felt could adequately explain their different breathing patterns. He concluded that the different size, shape and position of the abdomen in relation to the lung fields in the cow and horse were probably more important in determining which breathing strategy was utilized.

Some potentially important differences do exist between the horse and cow in regard to the position of the diaphragm relative to the abdominal and thoracic cavities. In the horse, from costal attachments beginning on the ventral aspects of the 8th, 9th, and 10th ribs and continuing back, with increasingly more dorsal attachments, to the last rib (18th), the diaphragm domes deeply forward and is compressed laterally. The general direction of the muscle on a midline section as it extends from the lumbar vertebrae to the xiphoid process is downward and forward. The flexures of the great colon and the liver fit into the concavity created by the dome of the diaphragm (Sisson, 1953). Thus in the horse, a large portion of the lungs lie dorsal to the diaphragm and the cranial part of the abdominal cavity. On the other hand, in the cow, the slope of the diaphragm is much greater. The upper limit of the costal attachment extends almost in a straight line from the last rib (13th), near the vertebral end, to the 8th rib, near the costo-chondral junction, and the sternum. On the midline, the diaphragm slopes obliquely to the level of the vena cava, then drops almost vertically (Sisson, 1953). The bulky rumen is situated immediately caudal to the diaphragm, and the bovine lung is shorter in the axial direction than that of the equine. Therefore, the lung fields are located immediately in front of the diaphragm and rumen.

It would seem that the anatomical arrangement of the lung fields dorsal to the abdominal cavity could easily influence the breathing strategy adopted by the horse. During inspiration, with the abdominal wall relaxed, lung inflation should be facilitated by a tendency for the heavy abdominal organs to fall away from the lung fields (Sorenson and Robinson, 1980). Facilitation of lung deflation during expiration would involve active contraction of the muscles in order to lift the abdominal viscera and overcome gravitational and inertial forces (Gallivan, 1981). Thus, in the quietly breathing horse, the abdomen appears to share the principal pumping duties with the diaphragm. In the cow during inspiration, diaphragmatic contraction moves the abdominal contents in a primarily caudal direction. During expiration, the abdominal viscera would tend to return passively to their more cranial resting position. Abdominal muscle contraction does not seem to offer any particular advantage under these circumstances, and the diaphragm appears to be the primary pump muscle in this species.

In the horse, it is possible that the abdominal muscles aid inspiration in another way as well. In other species, including man, the abdominal muscles exert an important influence on the action of the diaphragm. By contracting during expiration, the abdominal muscles displace the diaphragm into the thorax, lenghtening its fibers, thus placing it at a more advantageous position on its length-tension curve. If muscle contraction takes place at this longer operating length, the effectiveness of the diaphragm as a pressure generator is improved (Grassino et al., 1978; Kim et al., 1976). From the results of the present study, however, as the activation of the diaphragm is often delayed, it appears that at least during quiet breathing, the horse does not routinely take full advantage of this potentially favorable mechanical situation. However, it has been suggested that if a muscle actively shortens immediately after being stretched, it can perform more positive work at a given length than a muscle not previously stretched (Cavagna et al., 1968). Therefore, the diaphragm of a horse breathing with a delay in onset of inspiratory activity relative to inspiratory flow may also be operating at a mechanical advantage. It is possible that only during exercise or in other times of increased respiratory demand is the diaphragm activated when the length-tension characteristics are optimal. However, until investigations of the mechanical characteristics of the equine diaphragm are performed, such statements must remain strictly conjectural.

One possible explanation for the breathing strategy lies in the passive mechanics of the equine respiratory system. Leith and Gillespie (1971) measured pulmonary and chest wall compliance in paralyzed, anesthetized upright adult horses. Their data suggested that the equine chest wall, normalized to body weight is very stiff in comparison to other species, while lung elastic behavior is similar to that of other species. Furthermore, the resting volume of the chest wall is similar to the resting volume of the respiratory system. A stiff chest wall in a large animal is probably advantageous both to support locomotor function and to stabilize end-expiratory lung volume during postural changes. However, the elastic work of breathing in such a system will also be high. Many studies have supported the theory that an "optimal" breathing frequency and depth is chosen by each animal that minimizes the total work of breathing (Agostoni et al., 1959; Crossfill and Widdicombe, 1961; Mead, 1960; Otis et al., 1950). In comparison to the cow, a similarly sized animal, the normal horse breathes with a low respiratory rate and a large tidal volume, which would also contribute to high elastic work of breathing. It would follow that the horse would adopt a strategy of breathing that would minimize this elastic work. As proposed by Otis (1964), such a strategy would involve breathing around, rather than from, the relaxation volume of the respiratory system. In this case, the first part of inspiration can be passive, because work is recovered from the elastic energy stored during the latter active part of the previous expiration. In other words, by breathing lower than Vrx, energy obtained from the outward recoil of the chest wall is utilized during the first part of inspiration, allowing it to be passive initially. Thus, the abdominal muscles, by performing positive work during expiration, share the total work of breathing with the inspiratory muscles and by doing so, minimize the total elastic work of breathing.

In summary, this study has shown that the adult horse breathes substantially around, rather than from, Vrx by using a combination of active and passive inspiration and expiration. The central and peripheral control mechanisms of such a pattern are unknown at this time, but if determined could potentially aid the understanding of general neural mechanisms of the control of breathing.

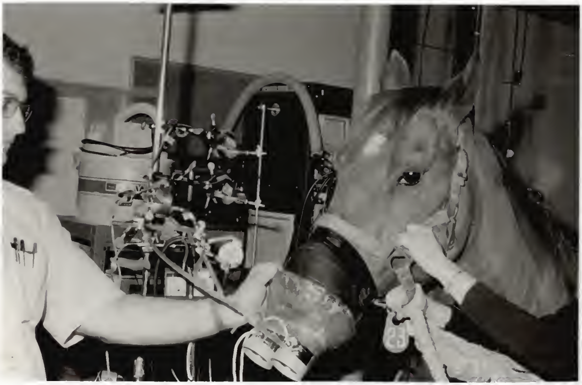

Figure 1-1. Adult horse with pneumotach-facemask system in place.

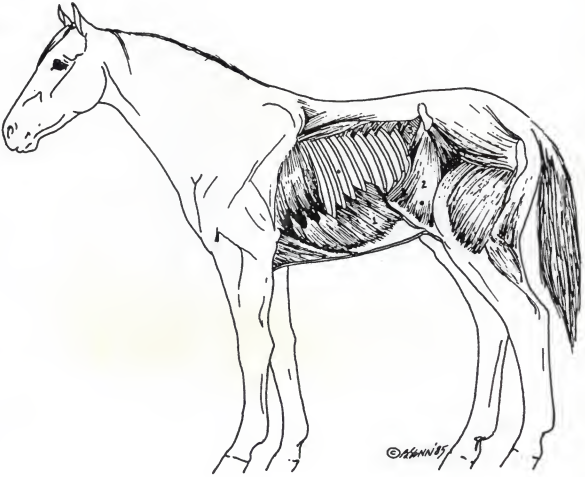

Figure 1-2. Abdominal and intercostal musculature of the horse. 1, External abdominal oblique muscle, cut away to reveal: 2, Internal abdominal oblique muscle. Dot denotes position of wire Eabd electrode. Fascia of external abdominal oblique muscle overlies internal abdominal oblique at level of electrode; 3, Transversus abdominus muscle. Dot in 11th intercostal space denotes position of wire Eint electrode.

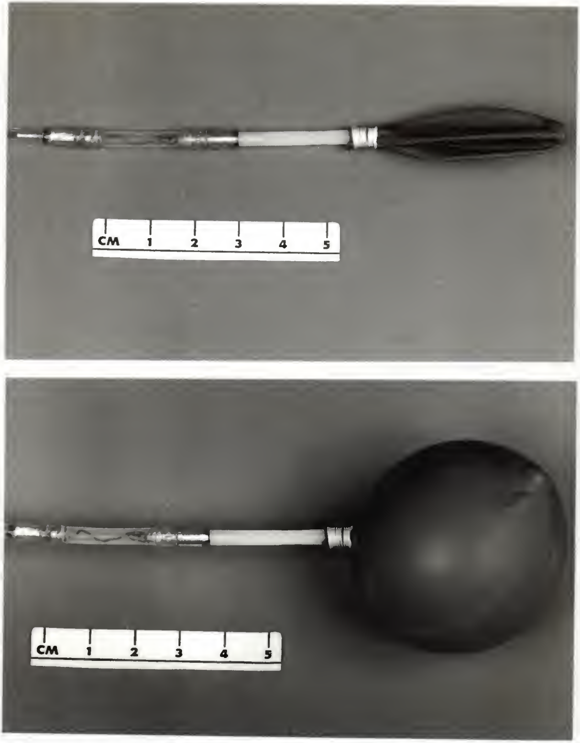

Figure 1-3. Intraesophageal bipolar silver Edi electrode with inflatable balloon. Top panel) Balloon deflated; Bottom panel) Balloon inflated.

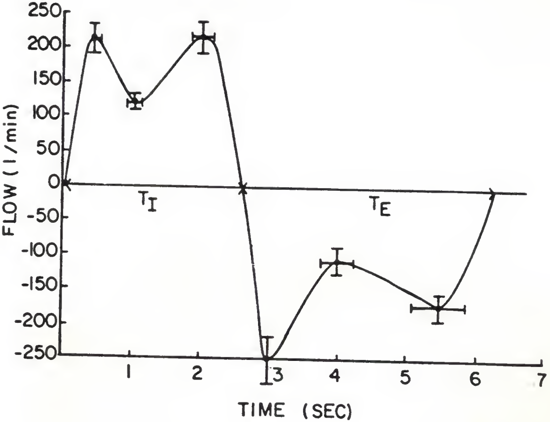

Figure 1-4. Composite breath of the adult horse. Points are means of peaks and dips of inspiratory and expiratory flow and the times at which they occurred (mean ± SEM). T_I is inspiratory time, T_E is expiratory time.

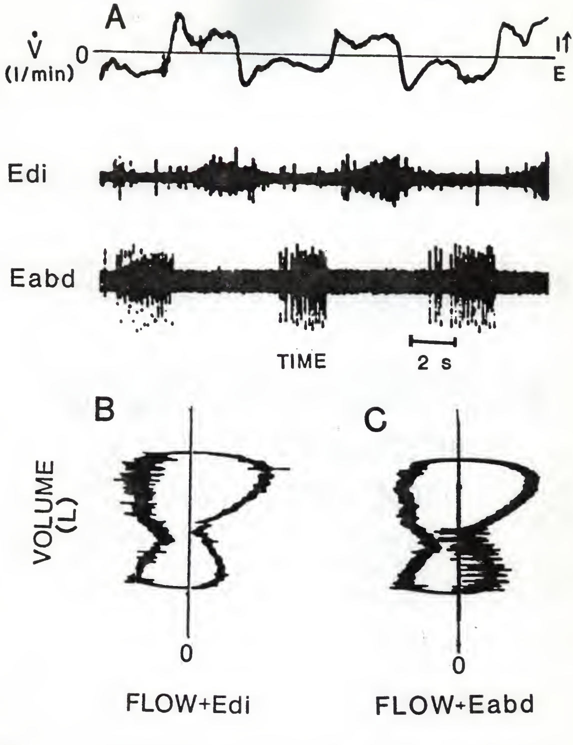

Figure 1-5. Representative flow, volume, and EMG tracings of horse #8. A) Flow ($\dot{V}$) and EMGs against time. Note lag in onset of EMGs relative to onset of inspiratory and expiratory flow and the persistence of Edi into expiration; B) Paintbrush flow-volume loop, with majority of Edi signal during second phase of inspiration; C) Paintbrush flow-volume loop with Eabd signal present during second phase of expiration.

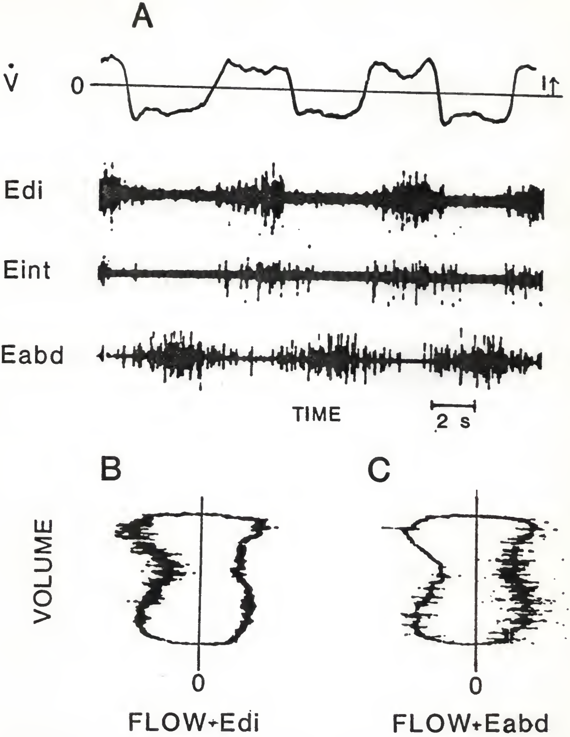

Figure 1-6. Representative flow, volume and EMG tracings of horse #6. A) Flow and EMGs plotted against time. Note persistence of Eabd into inspiration; B) Paintbrush flow-volume loop, with short delay in onset of Edi; C) Paintbrush flow-volume loop, with early onset of Eabd, and less biphasic expiratory flow pattern.

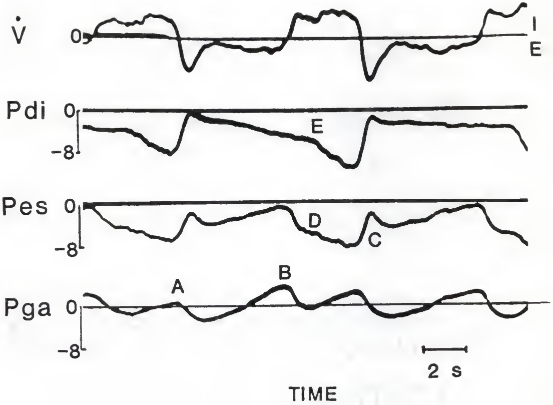

Figure 1-7. Representative flow, transdiaphragmatic, esophageal, and gastric pressure tracings in horse #4. Transdiaphragmatic pressure decreases through second part of expiration and first part of inspiration. Point A denotes inspiratory peak of Pga; Point B denotes expiratory peak of Pga; Point C denotes peak of Pes associated with first peak of expiratory flow; Point D represents less pronounced peak of Pes associated with first peak of inspiratory flow; Point E represents the point at which Pdi changed its slope of descent.

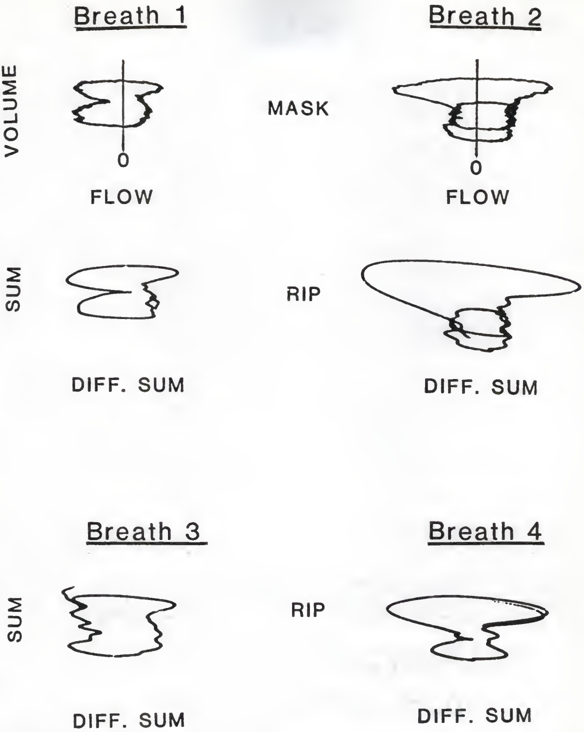

Figure 1-8. Pneumotach and RIP-generated flow-volume loops in the adult horse. Breath 1 and 2 compare loops generated by pneumotach to those obtained using respibands. Breath 3 and 4 loops were obtained using respibands without facemask in place. Biphasic inspiration and expiration are still obvious.

CHAPTER II
STATIC MECHANICS OF THE RESPIRATORY SYSTEM OF THE GROWING FOAL

Introduction

Although the mechanical properties of the respiratory system of several newborn animal species have been investigated, most studies have involved species that are smaller than the newborn infant, including the guinea pig (Gaultier et al., 1984), rat, rabbit, cat, dog, and pig (Fisher and Mortola, 1980); rat (Nardell and Brody, 1982), and fetal and neonatal dog (Agostoni, 1959). Only a few studies have described the respiratory mechanics of newborn species that are larger and more mature at birth than the human infant. Avery and Cook (1961) described the volume-pressure relationships of the respiratory system in the fetal, newborn, and adult goat, and there have been a few investigations in the neonatal calf (Kiorpes et al., 1978; Lekeux et al., 1984; Slocombe et al., 1982).

Despite numerous reports of pulmonary mechanics of both normal and diseased adult horses (Gillespie and Tyler, 1969; Gillespie et al., 1966; Mapleson and Weaver, 1969; McDonell and Hall, 1974; Muylle and Oyaert, 1973; Purchase, 1966; Robinson et al., 1975; Sorenson and Robinson, 1980; Willoughby and McDonell, 1979), little information is available regarding normal respiratory system mechanics in the immature horse. Although it has been postulated that the respiratory apparatus of newborn foals resembles that of newborn human infants and smaller mammals (Gillespie, 1975), there is no experimental evidence in support of this. The only description of the pressure-volume (P-V) characteristics of the live foal's respiratory system is hypothetical (Gillespie, 1975), based on extrapolations from data collected in other neonatal species. The only published values of normal lung volumes in foals are those of tidal volume and minute respiratory volume (Gillespie, 1975; Rossdale, 1969; Rossdale, 1970; Stewart et al., 1984).

Certain structural characteristics appear common to neonates of all species. A flexible, compliant chest wall is essential for uncomplicated delivery of a mammal through the birth canal. In addition, during the first hours following delivery, the presence of residual liquid in the lung interstitium has been found to substantially reduce lung compliance (Agostoni, 1959; Avery and Cook, 1961; Fisher and Mortola, 1980; Mortola, 1983c). Therefore, a high ratio of chest wall to lung compliance is thought to be a general characteristic of all newborn mammals (Mortola, 1983c). Unfortunately, these same underlying structural requirements can adversely affect gas exchange and the efficiency of ventilation in a number of ways. These adverse effects and the patterns and strategies of breathing selected by neonates to compensate for the limitations set by their immature mechanical characteristics will be discussed more fully in the following chapter.

Very few studies document the time frame or pattern of transition between neonatal and adult respiratory structure and function, and again, most of these report on findings from small mammals (Gaultier et al., 1984; Nardell and Brody, 1982). Lekeux et al. (1984) examined the effect of growth on selected pulmonary function values in awake Friesian cattle but did not measure chest wall compliance or lung volumes other than tidal volume and functional residual capacity. Even in humans, where reports are most plentiful, there are gaps in information concerning the functional development of the respiratory system, particularly in the child from a few weeks to school age (Polgar and Weng, 1979). One might expect that more precocious newborns of larger mammals, such as the horse, which need to stand and run shortly after birth, would make a rapid functional and structural transition to an adult-like respiratory system. It might be also be expected that the foal's respiratory system at birth would be more mature than that of many of the smaller newborn mammals, such as the rat, in which several of the developmental studies have been performed. However, from the work of Littlejohn and Van Heerden (1975), Rose et al. (1983), Rossdale (1970), and Stewart et al. (1984), it appears that at least some aspects of respiratory function in the neonatal foal are inferior to those of the older foal and adult horse. For example, from studies of the effect of administration of 100% oxygen to neonatal foals (Rose et al., 1983; Rossdale, 1970), it was concluded that right-to-left cardiopulmonary shunting is normally present during the first 3 days of life. In term-induced foals, the mean precentage of physiological shunt as a proportion of cardiac output was estimated to be 16% (Rose et al., 1983).

A transition from a neonatal to an adult breathing pattern might be expected to occur concurrently with mechanical changes in the respiratory system, but no information regarding this topic could be found in the literature. The purpose of the present study was to investigate the developmental changes in the mechanical properties of the respiratory system over time in a group of growing foals. In serial studies conducted several times between 24 hours of age and one year of age, P-V curves were generated and subdivisions of lung volume were measured. In addition to establishing normal baseline data for respiratory mechanics in foals of different ages, it was hoped that generation of these data in a neonate that is large and mature at birth could provide needed information in the field of comparative respiratory physiology.

Materials and Methods

Ten foals born over a two year period at the College of Veterinary Medicine, University of Florida, were utilized. Breed, gestational age, sex, and body weight at birth can be found in Table 2-1. All were sired by the same Thoroughbred

Table 2-1. Breed, gestational age, birth weight, and ages at which static mechanical measurements were made.

Foal #	Breed	Sex	Body Weight at Birth (kg)	Gestational Age (Days)	Ages when Studied (Days)
1	TBxQH	M	45.5	333	2,7,14,30,90,180,365 [21,60,290]
2	TB	M	35.0	323	2,9,30,90,180,365 [14,21,60,290]
3	TBxQH	F	39.5	326	2,9,16,30,90,180,365 [60,290]
4	TBxQH	F	40.0	335	14,30,90,180,365 [7,21,60,290]
5	TBxQH	M	31.8	355	14,30,90,180,365 [7,21,60,290]
6	TB	F	33.6	341	2,9,16[21,30]
7	TBxQH	F	44.0	333	8,16,30
8	TBxQH	F	43.2	320	2,9,16[30]
9	TBxQH	M	45.5	326	2

Table 2-1. continued

Foal #	Breed	Sex	Body Weight at Birth (kg)	Gestational Age (Days)	Ages when Studied (Days)
10	TB	M	43.2	347	9,28[3]
$\overline{X}$			40.13	333.9	
±SD			±5.06	±11.1	

Mean ($\overline{X}$) ± standard deviation (SD). Numbers in brackets are additional days on which awake breathing studies were performed (Chapter III).

stallion, which was of average height, weight, and conformation for the breed. The mares represented a number of different conformational types. Foals #3 and 8, and #4 and 9 were full siblings. The gestational ages ranged between 320-352 days, with a mean ± SD of 333.9 ± 11.1 days, which is normal for the equine, and all foals except #5 appeared of normal size and development for their gestational age. Foal #5 was small for gestational age due to chronic placental insufficiency in utero. In spite of his small size at birth, he was in good health and grew normally after birth to reach a normal size by two weeks of age. All foals were born spontaneously in a pasture; the births were usually unattended, but no obvious abnormalities associated with the birth process were noted.

Foals #1-5 were serially studied from the first day of life to one year of age. Ages at which respiratory mechanical measurements were made were 24-36 hours, day 7-9, day 14-16, day 30-32, 3 months, 6-7 months, and 12-13 months. Due to technical problems with the measurement techniques initially, and to an outbreak of equine influenza later, a complete set of data could not be collected on each of these foals during the first month of life (Table 2-1). Therefore, foals #4 and 5 were studied anesthetized for the first time at 14 days of age. All studies from 3 months to 1 year of age, however, were completed in these five animals. Foals #6-10 were studied during their first month only, on the days listed in Table 2-1. Foal #9 was studied on day 2 of age, but became septicemic following recovery from the anesthesia and died at two weeks of age. All foals were housed in a large pasture with their mothers until they were weaned (5-6 months of age), when they were moved to another pasture.

Prior to each anesthetized study, the foal's respiratory system and general health was assessed by physical examination, chest radiography, and a complete blood count. When evaluated together, these parameters were considered to accurately reflect the overall health of the foal and its respiratory system, in the absence of a post-mortem examination. In addition, each foal's height, girth and abdominal circumference, and body weight were measured and averaged for each study time to assess the overall growth pattern of this group of developing horses.

Anesthesia Protocol

In most foals of one month of age or less, prior to induction of anesthesia, cuffed silastic endotracheal tubes (7-11 mm I.D., 50-55 cm in length, Bivona Surgical) were passed via the external nares into the trachea and secured, using the technique described by Webb (1984). In four studies, the tube was passed through the oral cavity after induction of anesthesia because of difficulty encountered in passing the tube nasotracheally in the awake foal. All foals of 3 months of age or older were anesthetized prior to placement of a cuffed endotracheal tube (12-22 mm I.D.) through the mouth. Foals of 3 months of age or less were not fasted prior to the studies, but in all studies that followed weaning (5 months of age) the animals were not fed the morning of their study.

Two anesthetic protocols were utilized, depending on the foal's age. Animals from 24-36 hours to 3 months of age were initially anesthetized with pentobarbital sodium (15 mg/kg of body weight) administered intravenously over a 3-5 minute period. This dose and rate of administration was found necessary to avoid severe respiratory depression and occasional cardiac arrest in the younger subjects. If the measurement period extended past approximately 45 minutes, it was usually necessary to repeat one-half the dose to maintain adequate anesthesia. In most studies, serum pentobarbital levels were monitored as a part of a separate pharmacokinetic study. After a period of data collection on the spontaneously breathing, anesthetized foal, pancuronium sulfate (Pavulon, Organon, Inc.) was given intravenously (0.06 mg/kg) to induce respiratory muscle paralysis to perform respiratory mechanical measurements. When the respiratory efforts decreased in intensity, mechanical ventilation with a volume-cycled ventilator was instituted. Adequacy of ventilation was assessed by end-tidal CO_2 measurements (Beckman, LB-2 gas analyzer) and by occasional arterial blood gas determinations (Instrumentation Labs, model 813); and tidal volume and/or frequency of ventilation was adjusted according to the results obtained. Additional pancuronium doses were administered to maintain complete respiratory muscle relaxation. After completion of the anesthetized-paralyzed foal experiment (usually about 45 minutes), the foals were allowed to recover. Muscle paralysis was usually reversed by intravenous administration of neostigmine (1 mg/foal) at the end of the study. The time elapsed between induction of anesthesia and return to normal nursing behavior was usually 3 hours.

It was previously determined that foals 6 months of age or older require additional doses of pentobarbital to maintain an adequate level of anesthesia, and prolonged, rough recoveries often resulted. In order to avoid injuries during the recovery period, an alternate anesthetic regimen was instituted in the older foals. Anesthesia was induced with guaifenisin (glycerol guiacolate) and thiopental (2 gms/liter of GG) given as a continuous, rapid intravenous infusion until the desired level of anesthesia was reached. The usual dose required for induction of anesthesia was 80-100 mg/kg guaifenisin and 4 mg/kg of thiopental. Muscle relaxation was maintained by a slow continuous drip of the same solution. Muscle paralysis was induced with pancuronium and maintained in the same manner as in the younger animals.

Mechanical Measurements

All measurements were made while the foal was maintained in sternal recumbency, with the front legs tucked under the body and the head supported in a horizontal plane with the rest of the body (Fig. 2-1). In the younger foals, an upright sternal position was maintained by use of heavy wedges placed at the shoulder and hip. In the older, heavier animals, it was more difficult to achieve a totally sternal posture, and the animal's trunk was often tilted slightly toward the horizontal plane.

Airflow ($\dot{V}$) was measured using a Fleisch no. 2 heated pneumotachograph connected to the endotracheal tube via an adaptor with a side port used for measurement of airway opening pressure (Pao). A ± 5 cm H_2O differential pressure transducer (Validyne model MP-45) was used to measure the pressure drop across the pneumotachograph and this signal was electronically integrated to yield volume (Validyne integrator, model FV-156). The system was calibrated as described in Chapter I. The Pao was measured using both a ± 2 cm H_2O and ± 50 cm H_2O pressure transducer (Validyne model MP-45), for measurement of Pao either during tidal breathing or during quasi-static pressure volume maneuvers, respectively. The endotracheal tube and pneumotach were connected to the ventilator during mechanical ventilation and during the passive pressure-volume maneuvers, to a supersyringe or in the larger foals, an airblower. The connections were slightly modified for the one year studies to increase the diameter of the airway. The dead space of this equipment was 75 ml for the younger foals, and 110 ml in the older animals.

Esophageal pressure (Pes) was measured with a 7.5 cm long, hand-dipped, latex esophageal balloon filled with 1-2 ml of air. It was connected by teflon PFA tubing (Cole

Palmer Instrument Co.; 200 cm long, internal diameter 2 mm) to one side of a ± 50 cm H_2O differential pressure transducer (Validyne, model MP-45). The frequency response of the balloon-catheter system was tested using the method of Jackson and Vinegar (1979). A flat response in amplitude was observed to over 10 Hz and in phase to over 4 Hz. All pressure systems were calibrated before and after the studies using a water manometer. The balloon was positioned in the caudal part of the esophagus, a short distance from the cardia, to minimize the often prominent cardiac artifact frequently present during breathing under anesthesia. Prior to induction of paralysis, while the sternal, anesthetized animal was breathing spontaneously, the validity of the esophageal pressure measurement was tested using the airway occlusion technique (Baydur et al., 1982; Beardsmore et al., 1980; Milner et al., 1978). This involved occluding the airway opening at end-expiration and allowing the animal to perform an occluded inspiratory effort, while monitoring for any change in transpulmonary pressure (Ptp). If there was a substantial change in the Ptp baseline during the occlusion, the balloon was repositioned and/or the volume of air inside was adjusted until the baseline remained unchanged during the maneuver. The volume of air in the balloon and its position in the esophagus were then kept constant.

For the quasistatic pressure-volume (P-V) curves, pressure and volume signals were displayed on the X- and Y-axes, respectively, of a dual-beam storage oscilloscope

(Tektronix model 5113), and recorded on an 8-channel FM tape recorder (Vetter model D). Transpulmonary pressure (Ptp) was determined by electrical subtraction of Pes from Pao, transthoracic pressure (Pw) was determined by subtraction of the body surface pressure (Pbs) from Pes, and transrespiratory pressure (Prs) was recorded as the difference between Pao and Pbs. The relaxation volume of the respiratory system was defined as the resting volume reached following a large inflation and slow passive deflation. Under anesthesia and muscle paralysis, functional residual capacity (FRC) or end-expiratory lung volume (EEV) is equivalent to the relaxation volume of the respiratory system (Vrx). Total lung capacity (TLC) was defined as the lung volume at a Ptp of 30 cm H_2O, and residual volume (RV) as the lung volume at a Ptp of -30 cm H_2O. A schematic diagram of the equipment used during the P-V maneuvers is shown in Fig. 2-1.

Immediately preceding the generation of each P-V curve, a standard volume history was attained as the lungs were twice inflated to a Ptp of 30 cm H_2O and allowed to deflate passively to Vrx. In the studies of foals 3 months of age and less, slow inflations were accomplished by a large calibrated syringe 3 or 7 liters in volume, depending on the size of the foal. In foals 6 months of age or greater, curves were generated using a rheostat-controlled vacuum cleaner. Curves acquired using each of these methods were compared and did not appear to differ. In addition to providing a constant volume history for the curves, observation of the volume at the start and finish of these preliminary inflations helped to verify that potential measurement artifacts, such as electrical drift, were minimal. Following these maneuvers, the lungs were again slowly inflated to TLC, slowly deflated to RV, and then usually allowed to passively reinflate toward FRC. This sequence routinely took about 30-45 seconds. To observe the change in character of the inflation limb of the P-V curve when inflation took place from a low lung volume, in some studies, following completion of the curve, the lungs were reinflated from RV to TLC. At least 3 complete P-V curves were obtained per study. Inspiratory capacity (IC) and expiratory reserve volume (ERV) were measured from the P-V curves as the lung volume from FRC to TLC, and from FRC to RV, respectively. The lung volume at which the chest wall deflation curve crossed the Y-axis, the resting position or unstressed volume of the chest wall (0CW), was also measured. Compliance of the lungs (C_L), chest wall (C_W) and total respiratory system (C_{RS}) were measured as the slope of the linear part of the deflation limb of the appropriate P-V curve near FRC. The absolute volumes for RV and TLC were calculated with the addition of the measurements of FRC (see below). All lung volumes were corrected and reported in BTPS. Finally, the maximum and minimum value of Pw at TLC and RV, respectively, was recorded, as well as the value at FRC.

The FRC was measured in the paralyzed, anesthetized state using a modification of the closed system nitrogen (N_2) equilibration technique (Robinson et al., 1972) first described by Lundsgaard and Van Slyke (1918) for use in awake humans. After lung inflation to TLC and passive deflation to FRC, a large syringe and three-way stopcock containing a volume of oxygen similar to the inspiratory capacity of the subject was attached by way of the pneumotach to the endotracheal tube. While at FRC, the valve was turned and a total of 4 breaths were delivered to the foal using the entire contents of the syringe each time. The procedure took an average of 15 seconds to perform. At the end of the procedure, the syringe was returned to its original volume, sealed tightly and disconnected from the animal. The fraction of nitrogen in the syringe was measured using a N_2 analyzer (Med Science Electronics model 505). The FRC was calculated by the following equation:

$$FRC = V_S \times F_{N2}(end)/[F_{aN2} - F_{N2}(end)]$$

where V_S = volume of oxygen in syringe; $F_{N2}(end)$ = % nitrogen in the syringe at the end of the test; and F_{aN2} = % nitrogen in the alveoli at the start of the test. The F_{aN2} was assumed to be 80%. Corrections were made for the apparatus dead space (pneumotach and connectors, but not endotracheal tube = 75 or 110 ml, depending on animal's age), and for the dead space of the valve and tubing of the oxygen syringe (120 ml). No correction was made for any nitrogen washed out from body stores (Rahn et al., 1949).

The choice of the number of inflations (4) to be delivered to the foal during the FRC determinations was based on the work of Rahn et al. (1949), as well as by observation of the pattern of nitrogen equilibration measured by the rapidly responding nitrogen analyzer placed in line during the maneuvers. This was performed in representative animals of each age group. In all animals tested, equilibrium was reached at the end of the fourth breath, after which the N_2 concentration slowly, but steadily increased with each additional breath. A total of three FRC determinations were made per study and the results were averaged.

Means and standard deviations for absolute lung volume and compliance measurements were computed for all foals in each age group. Because the best normalizing factors for generating the most meaningful comparisons over time in the growing foal were not known, each measured value was normalized both to body weight and to lung volume (TLC and/or FRC). The mean of each absolute and normalized lung volume and compliance value in an age group was then compared to the means obtained in the other age groups. The calculations were performed at the facilities of the Southeast Regional Data Center located at the University of Florida, using the Statistical Analysis System (SAS Institute, 1982). Two-way analysis of variance and Tukey's Studentized Range test for multiple comparisons were performed on all data of the different age groups. Certain dimensionless relationships, such as C_W/C_L, were also compared using the same statistical tests for each age group. A statistically significant difference between two groups was defined by $P < 0.05$ for a two-tailed test. Linear regression analysis was performed with a minicomputer (Digital Equipment model PDP-11/23) using means of body weight and age as independent variables and the lung volumes and compliances as dependent variables. In addition, the data were transformed to base 10 logs for least squares regression analysis of allometric equations of the form $y = ax^b$, where y = any variable, a = the Y-intercept, or the extrapolated value for a 1 kg animal, x = body weight in kg., and b is the slope on a log-log plot. The values of the correlation coefficients (r) and the differences of the slopes were tested for significance for a two-tailed t test.

Results

The changes in body weight, height at the withers, girth and abdominal circumference observed in the neonatal foals studied during their first year of life are represented in Figs. 2-2 and 2-3. During the first 3 months of age, overall growth was most rapid, and from 3 months to 1 year of age, the slope of all lines became progressively less steep. At birth, the average height exceeded the girth and abdominal measurements by about 7 inches, but between 4-5 months of age, the height and girth curves intersected. During the rest of the study period, the girth continued to grow at a faster rate than height. Schematic

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representations of the changes made in body proportions during growth are illustrated in Figs. 2-4 to 2-9. From birth to 1 month of age, the most obvious change observed was a tremendous increase in muscle mass, particularly in the hindquarters and rump (Fig. 2-5 vs 2-4). From 1 month to 3 months of age, height, body weight, and trunk circumference all increased dramatically, but the foals at 3 months of age still retained a short-necked, long legged, immature appearance relative to the adult (Fig. 2-6 vs 2-9). From 6 to 12 months of age, the most obvious growth was in the trunk and neck, and the foals began to show more adult-like proportions (Figs 2-7 and 2-8). By one year of age, the foals had reached approximately 88% of their projected adult height but only 68% of their projected adult body weight. The growth from one year of age to adulthood involves a substantial increase in trunk length and depth, and body weight with only a relatively minor increase in height.

Neonatal Foal Static Mechanics

Representative quasi-static P-V curves generated in two 2-day-old foals are shown in Fig. 2-10, panels A and B. The means of the absolute lung volumes of the foals at 2 days of age obtained from the P-V curves are listed in Table 2-2, the mean volumes normalized to body weight are listed in Table 2-3, and the mean volumes normalized to TLC are listed in Table 2-4. In the newborn foal, TLC averaged 79.5 ± 4.5 ml/kg (mean ± SD), FRC averaged 32 ± 3.2 ml/kg, and RV

Table 2-2. Subdivisions of lung volume in the growing foal.

Age	n	BW (kg)	TLC (liters)	IC (liters)	FRC (liters)	ERV (liters)	RV (liters)	OCW (liters)
Day 2	4-5	40.4 ±5.2	3.23^{efg} ±.56	2.12^{efg} ±.42	1.26^{efg} ±.24	0.78^{fg} ±.19	0.50^{defg} ±.14	1.88^{efg} ±.22
Week 1	6	50.5 ±5.3	4.14^{efg} ±.43	2.56^{efg} ±.31	1.65^{efg} ±.22	0.97^{fg} ±.24	0.68^{efg} ±.17	2.20^{efg} ±.30
Week 2	6	58.0 ±7.13	4.54^{efg} ±.58	2.70^{efg} ±.38	1.85^{fg} ±.19	1.12^{fg} ±.20	0.73^{efg} ±.13	2.50^{fg} ±.27
Month 1	7	75.8 ±9.4	5.29^{fg} ±.72	3.18^{fg} ±.51	2.11^{fg} ±.34	0.99^{fg} ±.32	1.12^{fg} ±.18	2.73^{fg} ±.22
Month 3	5	136.6 ±13.4	7.04^{fg} ±.62	4.32^{fg} ±.36	2.72^{fg} ±.32	1.21^{fg} ±.28	1.51^{fg} ±.35	3.35^{fg} ±.31
Month 6	5	212.5 ±25.0	13.47^{g} ±1.9	8.67^{g} ±1.18	4.79^{g} ±.87	2.49^{g} ±.40	2.28 ±.52	5.20^{g} ±.94
Month 12	5	315.9 ±26.8	21.36 ±1.69	14.98 ±1.13	6.33 ±.63	3.65 ±.42	2.69 ±.38	7.12 ±.98

Values are means ± SD.
BW = Body weight, TLC = Total lung capacity, IC = Inspiratory capacity, FRC = Functional capacity, ERV = Expiratory reserve volume, RV = Residual volume, OCW = Resting volume of chest wall. e = value significantly less than value at 3 months, f = value significantly less than value at Month 6, g = value significantly less than value at 1 year of age ($p < 0.05$).

Table 2-3. Lung volumes normalized to body weight of foals from Day 2 to 1 year of age.

Age	n	TLC (ml/kg)	IC (ml/kg)	FRC (ml/kg)	ERV (ml/kg)	RV (ml/kg)	OCW (mg/kg)
2 days	4-5	79.5 ±4.5	50.9 ±5.5	32.0 ±3.2	19.2 ±2.8	12.8 ±3.8	46.6 ±1.7
1 week	6-7	83.2 ±4.7	50.6 ±4.0	33.1 ±3.2	19.0 ±3.8	14.0 ±4.4	44.6 ±1.2
2 weeks	6-7	80.6 ±6.7	46.6 ±5.2	33.0 ±2.5	19.2 ±2.4	13.2 ±3.6	44.5 ±2.8
Month 1	7	70.6 ±12.1	42.4 ±7.5	28.2 ±5.8	13.3^{abc} ±4.5	15.0 ±3.1	36.4^{abc} ±5.0
Month 3	5	52.2^{abcdg} ±8.6	32.0^{abcg} ±5.4	20.1^{abcd} ±3.4	9.1^{abc} ±2.8	11.1 ±2.3	24.8^{abcd} ±3.3
Month 6-7	5	63.7^{abc} ±8.5	41.0 ±5.5	22.6^{abc} ±3.9	11.8^{abc} ±2.2	10.7 ±1.7	24.7^{abcd} ±4.3
Month 12-13	5	67.9^{b} ±6.8	47.7 ±4.5	20.1^{abcd} ±2.4	11.7^{abc} ±1.9	8.5^{d} ±0.9	22.6^{abcd} ±3.4

TLC = Total lung capacity, IC = Inspiratory capacity, FRC = Functional residual capacity, ERV = Expiratory reserve volume, RV = Residual volume, OCW = Resting volume of chest wall. a = value significantly less than value at day 2, b = value significantly less than value at week 1, c = value significantly less than value at week 2, d = value significantly less than value at 1 month, e = value significantly less than value at Month 3, f = value significantly less than value at Month 6, g = value significantly less than value at 1 year of age ($p < 0.05$).
Values are means ± SD.

Table 2-4. Lung volumes normalized to total lung capacity (TLC) or functional residual capacity (FRC).

Age	n	FRC/TLC (%)	ERV/TLC (%)	RV/TLC (%)	OCW/FRC (%)	OCW/TLC (%)
Day 2	4	39.2 ±2.0	24.9 ±2.8	14.1^{d} ±2.4	1.51 ±0.12	58.8 ±5.0
Week 1	6	39.8 ±3.5	23.0 ±5.4	16.8 ±5.4	1.34 ±0.08	53.5 ±6.6
Week 2	6	41.0 ±2.1	24.6 ±3.1	16.4 ±4.5	1.35 ±0.05	55.4 ±1.7
Month 1	7	39.9 ±4.1	18.4^{ac} ±3.7	21.7 ±5.0	1.31 ±0.13	52.0 ±4.1
Month 3	5	38.6 ±2.2	17.2^{ac} ±4.5	21.40 ±4.5	1.24^{a} ±0.13	47.9^{a} ±5.5
Month 6-7	5	35.4 ±3.5	18.5^{c} ±1.4	16.8 ±2.8	1.09^{abcd} ±0.6	38.6^{abcde} ±2.5
Month 12	5	29.6^{abcde} ±1.2	17.1^{ac} ±1.3	12.5^{de} ±1.3	1.12^{abcd} ±.10	33.4^{abcde} ±3.9

RV = Residual volume, OCW = Resting volume of chest wall. a = value significantly less than (<) day 2 value, b = value significantly < week 1 value, c = value significantly < week 2 value, d = value significantly < 1 month, e = value significantly < 3 months. Values are means ± SD.

averaged 12.8 ± 3.8 ml/kg. The volume at the resting position of the chest wall (OCW) in the newborn foal was 46.6 ± 1.7 ml/kg. The ratio of FRC/TLC was 39.2 ± 2.0%, of RV/TLC was 14.1 ± 2.42%, of OCW/TLC, 58.8 ± 5.0%, and ERV/TLC was 24.9 ± 2.8%. Compliance values for the newborn foal are listed in Table 2-6 and 2-7. Lung compliance in the newborn foal averaged 0.152 ± 0.044 L/cmH_2O or 3.60 ± 0.67 ml/cmH_2O/kg, chest wall compliance was 0.129 ± 0.03 L/cmH_2O or 3.18 ± 0.60 ml/cmH_2O/kg, and total respiratory system compliance was 0.071 ± 0.02 L/cmH_2O or 1.71 ± 0.24 ml/cmH_2O/kg. Esophageal or transthoracic pressure at TLC averaged 10.6 ± 3.9 cm H_2O. A typical P-V curve obtained in the neonatal foal when lung inflation to TLC took place from RV is shown in Fig. 2-11, panel A.

Comparisons of Lung Volumes during Development

Means and standard deviations of subdivisions of lung volume for all age groups studied are presented in Table 2-2, and the relationships between them are depicted in Fig. 2-12. Table 2-3 and Fig. 2-13 illustrate the observed changes in lung volumes normalized to body weight associated with growth and Table 2-4 and Fig. 2-14 illustrate the changes in the same volumes normalized to TLC. Regression equations relating the means of the major lung volume subdivisions to body weight and age are listed in Table 2-5. All lung volumes increased linearly with body weight and age ($P < 0.001$). When the lung volumes were normalized to body weight (Table 2-3), there were no significant changes in

Table 2-5. Linear regression equations describing lung volume and compliance parameters as functions of body weight and age.

Parameter	Intercept	Slope	Correlation Coefficient (r)	Level of Significance for Slope $\neq 0$*
TLC(L) = f(BW)	0.339	0.064	0.99	$p = 0.00001$
IC(L) = f(BW)	-0.230	0.045	0.98	$p = 0.00004$
FRC(L) = f(BW)	0.652	0.018	0.99	$p < 0.00001$
RV(L) = f(BW)	0.337	0.008	0.98	$p = 0.00005$
OCW(L) = f(BW)	1.23	0.018	0.99	$p < 0.00001$
C_L(L/cmH_2O) = f(BW)	-0.045	0.004	0.97	$p = 0.00002$
C_W(L/cmH_2O) = f(BW)	0.068	0.001	0.98	$p = 0.00003$
C_{RS}(L/cmH_2O) = f(BW)	0.032	0.001	0.98	$p = 0.00005$

Table 2-5. continued

Parameter	Intercept	Slope	Correlation Coefficient (r)	Level of Significance for Slope $\neq 0$*
TLC(L) = f(age)	3.51	0.050	0.99	$p < 0.00001$
IC(L) = f(age)	1.99	0.036	0.99	$p < 0.00001$
FRC(L) = f(age)	1.58	0.014	0.98	$p = 0.00003$
RV(L) = f(age)	0.76	0.006	0.95	$p = 0.00053$
OCW(L) = f(age)	2.16	0.001	0.99	$p = 0.00001$
C_L(L/cmH_2O) = f(age)	0.161	0.003	0.99	$p = 0.00002$
C_W(L/cmH_2O) = f(age)	0.122	0.001	0.99	$p < 0.00001$
C_{RS}(L/cmH_2O) = f(age)	0.073	0.001	0.99	$p < 0.00001$
BW(KG) = f(age)	50.9	0.776	0.99	$p = 0.00001$

TLC = total lung capacity, IC = inspiratory capacity, FRC = functional residual capacity, RV = residual volume, OCW = resting volume of chest wall, C_L = lung compliance, C_W = chest wall compliance, C_{RS} = total respiratory system compliance.

*Level of significance for two-tailed test.

TLC/kg, IC/kg or FRC/kg until 3 months of age, when all 3 values reached a mimimum. From 3 months to 1 year of age, TLC slowly increased, primarily as a result of an increase in IC/kg. The average TLC/kg at 1 year of age was still significantly smaller than at day 7, resulting largely from a consistently low FRC/kg (20.1 ml/kg). Functional residual capacity remained a relatively constant percentage of TLC (35.4 - 39.2%) until 1 year of age, when FRC/TLC fell to 29.6 ± 1.2%. At one month of age, ERV/kg was significantly less than the values measured at all the younger ages and although there was a trend toward a further decrease from 3 months to 1 year, the differences were not significant. The ERV/TLC showed a similar trend. There were no clear-cut trends associating RV/kg or RV/TLC with growth; the only significant differences were observed at 1 year of age, when RV/kg and RV/TLC were lower than the values obtained at 1 month, and at 1 and 3 months, respectively; and at day 2, when RV/TLC was significantly lower than at month 1. After remaining constant during the first month of age, OCW/kg progressively decreased from 1 month to 1 year of age. This trend was also reflected in the ratios of OCW/FRC and OCW/TLC, which also were significantly lower in the older foals than in the newborns.

Comparisons of Compliance Values During Growth

Absolute and normalized values for C_L and C_{RS} for all age groups are listed in Table 2-6, and those for C_W are listed in Table 2-7. Lung, chest wall, and total respiratory

Table 2-6. Lung and total respiratory system compliance in growing foals.

Age	n	C_L (L/cmH$_2$O)	C_L/KG (ML/cmH$_2$O/kg)	C_L/FRC (L/cmH$_2$O/L)	C_{RS} (L/cmH$_2$O)	C_{RS}/KG (ML/cmH$_2$O/kg)	C_{RS}/FRC (L/cmH$_2$O/L)
Day 2	5	0.15^{fg} ±0.04	3.60 ±0.67	0.12^{g} ±0.01	0.07^{efg} ±0.02	1.71 ±0.24	0.056 ±0.005
Week 1	7	0.26^{fg} ±0.09	5.03 ±1.57	0.17 ±0.05	0.09^{fg} ±0.02	1.71 ±0.17	0.056 ±0.010
Week 2	7	0.25^{fg} ±0.09	4.40 ±1.48	0.16 ±0.03	0.09^{fg} ±0.01	1.48 ±0.16	0.050 ±0.003
Month 1	7	0.29^{fg} ±0.11	3.84 ±1.25	0.15 ±0.06	0.10^{fg} ±0.01	1.29^{ab} ±0.23	0.050 ±0.006
Month 3	5	0.32^{fg} ±0.07	2.36^{b} ±0.71	0.12^{g} ±0.02	0.12^{fg} ±0.01	0.85^{abcd} ±0.19	0.045 ±0.005
Month 6	5	0.77^{g} ±0.14	3.69 ±0.88	0.18 ±0.06	0.19^{g} ±0.04	0.92^{abcd} ±0.21	0.044 ±0.009
Year 1	5	1.41 ±0.53	4.52 ±1.84	0.24 ±0.06	0.31 ±0.01	0.99^{abc} ±0.07	0.053 ±0.005

C_L = lung compliance; C_{RS} = respiratory system compliance.

a = value significantly < day 2, b = value significantly < 1 week, c = value significantly < 2 weeks, d = value significantly < 1 month, e = value significantly < 3 months, f = value significantly < 6 months, g = value significantly < 1 year ($p < 0.05$). Values are means ± SD.

Table 2-7. Chest wall compliance and maximum transthoracic pressure of growing foals.

Age	n	C_W (L/cmH_2O)	C_W/KG ($ml/cmH_2O/kg$)	C_W/FRC ($L/cmH_2O/L$)	C_W/TLC ($L/cmH_2O/L$)	C_W/C_L	P_W(TLC) (cmH_2O)
Day 2	5	0.13^{efg} ±0.03	3.18 ±0.60	0.10 ±0.03	0.043 ±0.007	0.96 ±0.23	10.6^{bcdefg} ±3.9
Week 1	7	0.13^{efg} ±0.03	2.65 ±0.40	0.09 ±0.02	0.034^{a} ±0.007	0.58^{a} ±0.22	20.0^{fg} ±5.9
Week 2	7	0.13^{efg} ±0.03	2.30^{a} ±0.31	0.07^{a} ±0.01	0.030^{a} ±0.005	0.61^{a} ±0.33	19.2^{fg} ±6.2
Month 1	7	0.15^{fg} ±0.03	2.06^{ab} ±0.46	0.08 ±0.02	0.031^{a} ±0.004	0.59^{a} ±0.22	19.4^{fg} ±3.0
Month 3	5	0.19^{fg} ±0.01	1.38^{abcd} ±0.19	0.07^{a} ±0.01	0.029^{a} ±0.002	0.61^{a} ±0.12	19.2^{fg} ±3.1
Month 6	5	0.28^{g} ±0.05	1.33^{abcd} ±0.22	0.06^{a} ±0.01	0.022^{abcde} ±0.015	0.38^{a} ±0.09	29.7 ±1.0
Year 1	5	0.44 ±0.01	1.41^{abcd} ±0.11	0.08^{a} ±0.02	0.022^{abcde} ±0.002	0.34^{a} ±0.10	34.0 ±4.0

Values are means ± SD.

C_W = chest wall compliance. C_W/C_L = ratio of chest wall to lung compliance. P_W(TLC) = maximum transthoracic pressure at TLC. a = value significantly < the value at Day 2, b = value significantly < value at 1 week, c = value significantly < than that at Week 2, d = value significantly < than that at 1 month, e = value significantly < than that at 3 months, f = value significantly < than that at 6 months, g = value significantly < than that at 1 year ($p < 0.05$).

system compliances increased linearly with both age and body weight (Table 2-5). When normalized to body weight, C_L showed little change with increasing age, with the exception of the value at 3 months of age, which was significantly lower than that measured at 1 week of age (Table 2-6 and Fig. 2-15, panel A). Specific lung compliance (C_L/FRC) was significantly lower at both day 2 and 3 months of age than at 1 year of age (Table 2-6 and Fig. 2-15, panel B). Chest wall compliance on a per kg basis showed a consistent decrease during the first 3 months of growth, but there were no significant differences between the mean value obtained at 3 months and those obtained in the older foals (Table 2-7 and Fig. 2-17, panel A). The increased stiffness of the chest wall in the older foals is easily appreciated from comparison of representative chest wall curves of the newborn foal (Fig. 2-10, panels A and B) and yearling (Fig. 2-10, panels C and D). Specific chest wall compliance (C_W/FRC) and C_W/TLC showed similar, but less pronounced trends, with minimal changes observed after 2 weeks and 1 week of age, respectively (Table 2-7 and Fig. 2-17, panels B and C). However, the maximum Pw reached with lung inflation to TLC continued to increase from a value of 19.2 ± 3.1 cm H_2O at 3 months of age to 34.0 ± 4.0 cm H_2O at 1 year of age (Fig. 2-18, panel B). Both the mean elastic recoil pressure of the lungs at FRC (PtpFRC) and the minimum Pw observed at RV remained constant with increasing age, the latter value ranging from a mean of -15.77 cm H_2O at day 2 of age to

-17.1 cm H_2O at 1 year of age. The dimensionless ratio of C_W/C_L showed a progressive decrease over the study period from 0.960 ± 0.232 at day 2 of age to 0.343 ± 0.097 at 1 year of age (Table 2-7, Fig. 2-18A). Changes in C_{RS}/kg during growth paralleled those associated with C_W/kg. After a continuous decrease in C_{RS}/kg from newborn to 3 months of age, there were no further changes noted (Table 2-6 and Fig. 2-16). When normalized to FRC, no significant changes in C_{RS} were noted during the entire study period (Table 2-6).

Allometry

The log-log relationships between lung volumes and body weight, and between compliances and body weight, are illustrated in Figs. 2-19 and 2-20, respectively. The allometric equations are listed in Table 2-8. During the growth period studied, with the exception of C_L and IC, the slopes of all lung volumes and compliance values as a function of age were all substantially less than unity.

Discussion

In this study, the developmental changes in the static mechanical properties of the equine respiratory system during the first year of life were investigated. As very few studies had been conducted on the mechanics and function of the normal respiratory system of the neonatal foal, it was not clear how much the foal shared in common with other neonatal animals in regard to pulmonary mechanics and function. From the results of this study, it appears that

Table 2-8. Allometric equations describing lung volume and compliance parameters as functions of body weight (BW) in kg, according to equation $y = ax^b$.

Parameter	Intercept a	Slope b	Correlation Coefficient r	Level of Significance for b Different than 0
TLC(L) = f(BW)	0.131	0.863	0.98	$p < 0.0001$
IC(L) = f(BW)	0.068	0.904	0.98	$p < 0.0001$
FRC(L) = f(BW)	0.085	0.742	0.99	$p < 0.0001$
RV(L) = f(BW)	0.029	0.807	0.99	$p < 0.0001$
OCW(L) = f(BW)	0.198	0.608	0.99	$p < 0.0001$
C_L(L/cmH_2O) = f(BW)	0.005	0.926	0.95	$p < 0.001$
C_W(L/cmH_2O) = f(BW)	0.013	0.576	0.96	$p < 0.001$
C_{RS}(L/cmH_2O) = f(BW)	0.006	0.653	0.96	$p < 0.001$

some of the mechanical properties of the respiratory system of the foal are more developed at birth than those of other species. However, in the transition to adulthood, the developing respiratory system of the foal followed certain trends commonly observed during maturation (growth) in the smaller neonatal species, but differed in others.

Comparison of the Neonatal Foal to Other Neonatal Species

Lung volumes. The values for lung volumes obtained in this study for the anesthetized 2-day-old neonatal foal are similar to those obtained in a number of other animal species when normalized to body size. In a study of passive respiratory mechanics in anesthetized, supine newborn rats, guinea pigs, rabbits, cats, dogs, and pigs, Fisher and Mortola (1980) reported that FRC as a function of body weight appeared to be remarkably constant between newborns of different species. In human infants, FRC has also been shown to be closely correlated with the cube of the height of the infant or child, as the slope of log-log plot of FRC as a function of height was equal to 2.86 (Cook et al., 1958). On a per kg basis, Fisher and Mortola (1980) found FRC to range between 9.08 ± 4.2 ml/kg (mean + SD) in the newborn guinea pig to 50.19 ± 8.32 ml/kg in the kitten, with the puppy, rabbit, and pig all with values between 26.9 and 35.9 ml/kg. Gaultier et al. (1984) found that FRC/kg was about 20 ml/kg in the two day old guinea pig. In a study of respiratory mechanics of the anesthetized neonatal calf, Slocombe et al. (1982) reported that FRC/kg averaged 40.2 ±

9.0 (mean ± SD) ml/kg. Thus the mean value of 32.0 ± 3.2 ml/kg in the neonatal foal in the present study is within the range reported in a number of other species. Reports of FRC as a percentage of TLC have ranged from 29.8% in neonatal guinea pigs (Gaultier et al., 1984) to 48% in the 3-8 day old rat (Fisher and Mortola, 1980), and 51 ± 5% in the neonatal calf (Slocombe et al., 1982). In the puppy, FRC/TLC was found to average 30% in one study (Fisher and Mortola, 1980) and 20.1% in an earlier one (Agostoni, 1959). As all of these studies were performed in anesthetised subjects with the respiratory muscles relaxed, FRC was most likely very similar to Vrx. It is important to remember that FRC /TLC may be considerably higher in the awake neonate. For example, the Vrx of the human infant is estimated to be very low, 15 - 20% of TLC (Agostoni and Mead, 1964), while FRC/TLC measurements in the awake infant are closer to 40 - 45% (Agostoni and Mead, 1964; Polgar and Weng, 1979). This is due to the active maintenance of an elevated end-expiratory lung volume above Vrx. Several different mechanisms have been proposed to explain this neonatal breathing strategy. These include upper airway and diaphragmatic braking of expiratory flow, and a high frequency of breathing in a system with a relatively long time constant (Kosch et al., 1985a; Kosch et al., 1985b; Mortola et al., 1982; Olinsky et al., 1974). Although there is some evidence to suggest that certain small neonatal species utilize some of these strategies (England et al., 1985; Mortola et al., 1985), in many other neonatal species, including the foal, the extent of the utilization of these strategies during awake breathing is not known. This subject will be further addressed in Chapter III.

From the configuration of the quasi-static P-V curve of the chest wall (Fig. 2-10, panels A and B), it appears that RV in the neonatal foal, as in other neonates, is determined primarily by airway closure rather than by chest wall stiffness. The configuration of a typical P-V curve generated by lung inflation to TLC from RV (Fig. 2-11) is also supportive of the idea that a substantial amount of airway collapse is present at RV in the neonatal foal. Considerably higher inflation pressures are observed during the first part of the inflation from RV compared to from FRC, suggesting that a number of airways are reopened during inflation from a low lung volume. Residual volume in the neonatal foal (12.8 ± 3.8 ml/kg or 14.1 ± 2.4% of TLC) was found to be lower than that reported by Slocombe et al. in the neonatal calf (22 ± 6 ml/kg or 28 ± 6% of TLC), but was similar to the ratio of RV to TLC described in puppies (Agostoni, 1959). Because of problems with methodology in the smaller species, RV has not been reported for a number of neonatal species. Although it was speculated by Polgar and Weng (1979) that in human infants RV/TLC should be relatively large as a result of both a fairly small TLC and an increased tendency for airway collapse in the neonatal lung, this was not found to be the case in the neonatal foal.

The reported values for the resting volume of the chest wall of newborn species have ranged from 39% of TLC in the puppy (Fisher and Mortola, 1980) to 80 ± 8% of TLC in the calf (Slocombe et al., 1982). However, values for 0CW/TLC in the rat, rabbit, cat, and pig (Fisher and Mortola, 1980) all have been 61 - 63%, which is similar to the value of 58.8 ± 5% reported in this study for the foal.

Pressure-volume relationships. Although compliance values of the neonatal foal respiratory system are discussed separately from the lung volumes, it must be remembered that the two parameters are interdependent. The elasticity of the chest wall plays an important role in determination of FRC. If the chest wall is very compliant, it may not generate sufficient outward recoil force to balance the tendency of the lungs to recoil inward, resulting in a low resting lung volume which may potentially interfere with gas exchange and the efficiency of ventilation. From observation of the general shape of the P-V curves of the lungs and chest wall, it is also obvious that compliance values may vary considerably depending on the lung volumes at which they are measured. Therefore, for the sake of meaningful comparisons, it is important to make these measurements at a specified location, usually, by convention, a tidal volume above FRC. Thus, the compliance values reported reflect only a small portion of the overall pressure-volume behavior of the respiratory system.

Lung compliance normalized to body weight (Table 2-6) was similar to the values reported previously for other neonatal species, being somewhat higher than those reported in the immature rat, rabbit, and pig (Fisher and Mortola, 1980), calf (Slocombe et al., 1982), and human infant (Gerhardt and Bancalari, 1980; Hjalmarson, 1974; Swyer et al., 1960) but slightly lower than those of the kitten and dog (Fisher and Mortola, 1980). There are fewer reports of specific lung compliance (C_L/FRC) in neonatal animals. Like FRC, the relation between both lung and body size and lung compliance appears to be quite constant over a wide range of sizes (Cook et al., 1958; Fisher and Mortola, 1980, 1981).

A relatively soft, flexible chest wall is obviously beneficial, and probably obligatory, for an uneventful delivery of a mammal through the narrow birth canal (Mortola, 1983c). A high chest wall compliance has been confirmed in all neonatal animal species examined to date and in the human infant. Because of obvious experimental limitations, few studies have actually documented C_W in relaxed human infants. In one study in which measurements were made on preterm and term mechanically ventilated infants (Gerhardt and Bancalari, 1980) C_W/kg averaged 4.2 ml/cm H_2O in the term babies and 6.4 ml/cm H_2O in the premature infants ($P < 0.001$). Values in the newborn rats, rabbits, cats, dogs, and pigs ranged between 6.1 ± 2.7 (mean ± SD) ml/cmH_2O/kg (dog) and 12.23 ± 1.12 ml/cmH_2O (cat). Slocombe et al. (1982) found C_W/kg to be 8.85 ±2.44 (mean ±

SEM) in a group of neonatal calves, and Avery and Cook (1961) found values in two 3-day-old goats to be 6.15 and 15.4 cmH_2O/kg. The average value obtained for C_W in the 2-day-old foal was only 3.18 ± 0.60 ml/cmH_2O (mean ± SD), quite a bit lower than that recorded for the other neonatal species. The C_W/C_L was also low in comparison to other neonatal species. The reason for the discrepency between the foal and the other species, including the calf which has a body size similar to that of the foal, is not immediately obvious. However, as dystocia is very uncommon in the mare, it is apparent that if this structural characteristic is common to all neonatal foals, it interferes little with the birth process.

Changes in Respiratory Mechanics During Growth

Choice of normalizing factors. In order for meaningful comparisons to be made between animals of different sizes, it is frequently necessary to normalize values. In respiratory mechanics, body weight, lung weight (LW), height, or lung volumes, usually FRC or TLC, have been the most commonly used parameters. In comparison of animals of different sizes but of the same age, use of either lung or body weight for normalization should yield the same results, for LW/BW ratio appears to be constant between species (Fisher and Mortola, 1981). In the growing animal, however, this is not the case, as LW/BW decreases with age (Fisher and Mortola, 1980 and 1981; Gaultier et al., 1984; Mortola, 1983c). Thus, the process of dysanaptic growth, with certain parts of the body growing at different rates than others, makes selection of the most appropriate normalization factors during growth studies difficult. As no one factor can probably tell the complete story, calculation and comparison of several different ratios may provide more insight into the relationships between the parameters and growth. In the case of variables normalized to body weight, the weights of many body components having nothing in common with the mechanical properties of the lung are included. In the adult horse, these body parts would include a large, heavy skull, long muscular neck and heavily muscled legs, while in the newborn foal a much smaller, lighter head, short neck, and thin legs lacking in muscular development would be included. Therefore, BW may be more influenced by the relative growth of other structures, such as the muscles and bones, than by lung growth (Fisher and Mortola, 1981). On the other hand, Fisher and Mortola (1980) suggested that BW may be a more appropriate normalizing factor than FRC when the chest wall is of particular interest, because the structure of the whole body and not just the lung is important for C_W determination. In addition, both C_W and OCW contribute to FRC. Mead (1961) commented that none of the lung volume subdivisions were suitable for normalization of C_L in terms of lung size because each depended on elastic properties of the lung as well as the size of the lung. He instead suggested that the best reference was probably lung weight as predicted from body height or weight, as he felt there would be less variability inherent in the measurements. The FRC/TLC ratio is also compliance-dependent and only provides information on the relative subdivision of lung volumes. The FRC/LW ratio provides some information on the density of the lung, which might be of interest in studies of lung maturation (Mortola, 1983c), depending on the purpose of the study. Because of these limitations, whenever possible, Mortola (1983c) has suggested calculation of dimensionless parameters, such as C_W/C_L, which can be compared among species without normalization.

In the present studies, because the foals were not terminated at the end of each experiment, and no published information was available relating lung size to body size in the horse, lung size could not be used as a normalization parameter. Instead, both lung volume, including TLC and FRC, and body weight were used to normalize the respiratory variables for comparison during growth.

Use of allometric equations. A relationship between a physiological or morphological variable and body mass is commonly referred to as an allometric function (Mortola, 1983b). Using allometry, animals are compared based on the assumption that structural and functional similarities exist, regardless of their body size. The equation, $Y = aM^b$ is commonly used, where Y is any variable, b is the slope of the log-transformed equation, a is the antilog of its intercept, and M is body mass. If a slope close to 1 is obtained, this signifies that the variable Y increases in direct proportion with M. In adult (Stahl, 1967) and newborn mammals (Fisher and Mortola, 1981) of different species, lung volumes (TLC, FRC) and compliance have been found to be directly proportional to body mass. If b is significantly greater than 1, Y is increasing at a faster rate than M, and if b is significantly less than 1, Y is increasing at a slower rate than M. Both oxygen consumption and minute ventilation have been found to be proportional to $M^{0.75}$ (Leith, 1976). If b is negative, this indicates that Y is decreasing as body mass increases, as in the case of breathing frequency, which is proportional to $M^{-0.26}$ (Stahl, 1967). Although Stahl (1967) commented that this type of analysis provides good results if applied to a size range of 100 times or more, it has been applied in the adult dog to only a 10-fold range of body weights, with apparently good results (Robinson et al., 1972). It is also possible to apply these equations to growing animals of the same species, as was done in the present study, to better appreciate the growth pattern of a particular system. In one such study of growing guinea pig, Gaultier et al. (1984) found that TLC was related to BW by the equation $TLC = 0.3\ BW^{0.69}$. This suggested that lung volume increased at a slower rate than body mass during maturation and supported the concept of dysanaptic growth. The present study was the first to describe the allometric functions relating respiratory variables to body weight in a large mammal during growth. The results will be discussed in the following section.

Changes in lung volume and compliance values during development. A linear regression equation was found between TLC, IC, FRC, and ERV and both body weight and age during the growth period from 2 days of age to 1 year of age (Table 2-5; $p < 0.001$). However, at 1 month (ERV) and 3 months (TLC, IC, FRC) of age, the lung volume/body weight ratios decreased significantly from their neonatal levels (Table 2-3). This phenomenon can also be appreciated from observation of the allometric plots (Fig. 2-19). Total lung capacity/kg and IC/kg increased again in the 6 month and 1 year studies, but FRC/kg and ERV/kg remained near the 3 month low value for the remainder of the study period. A significantly higher FRC/kg ratio has been observed in neonatal rats, rabbits, and cats (Fisher and Mortola, 1980), guinea pigs (Gaultier et al., 1984) compared to the corresponding adult, and a lower ratio has been observed in newborn puppies (Fisher and Mortola, 1980). However the trend in the foal of a decline and then an increase in lung volumes/kg ratios as described during growth has not been reported in other animals. However, few studies of this type have been performed, and none have closely or sequentially studied the respiratory system growth pattern during the first year of life in a large domestic animal species. There are several possible explanations for this finding: 1) There was some abnormality or disease process present in the foals studied at these age groups which influenced the results. 2) There was a problem with methodology. 3) The growth pattern of the lungs was different than that of the rest of the body.

In regard to the first possibility, the sample size studied was small at 3 months of age, and with repeated measurements in the same animals, 1 or 2 abnormal foals could have influenced the results a great deal. As an influenza virus had caused mild respiratory disease approximately 1 month prior to the 3 month study in 2 foals, this possibility needed to be ruled out. After evaluation of the lung volume/body weight data of each foal individually, it was clear that all 5 foals exhibited the same trends that were outlined above. The foals which had been sick showed no more decrease in lung volumes than the ones which had stayed healthy; in fact, the foal that showed the least drop in TLC/kg overall had been the sicker of the two animals. At the time of their 3 month study, all foals appeared very healthy, were afebrile, had normal complete blood counts, and had chest radiographs that were within normal limits.

Along the same lines, it may also be questioned whether this particular group of foals was representative of a normal population of foals. This question was addressed by comparison of the growth curves of the foals studied in this experiment with those generated in a much larger group of normal Thoroughbred foals at 8 different stud farms in England (Green, 1969). The results were strikingly similar, in spite of the fact that several of the foals in this study were only partially of Thoroughbred breeding. In both studies, growth was most rapid during the first 3 months of life, the amount of change in girth and height during that time period being only slightly less than the gains recorded in the following 9 month period. Green (1969) also described the changing ratio of height/girth measurements in the growing foal as demonstration of the proportional development of different parts of the body. He found, as in the present study, that the time of intersection of the two lines was between 4-5 months of age. Thus, it was concluded that overall, the growth pattern of the foals in the present study was normal for their breed type.

A second possibility that could explain the observed changes in lung volume/kg data is that there was a problem with methodology. Although both the technique of P-V curve generation and measurement of FRC have associated with them a large number of potential errors, it was thought unlikely that any of these accounted for the changes observed. First, the maneuvers were all done in the same way in all age groups, with only minor modifications for the increasing size of the foals. For example, an airblower was used in place of a large syringe to inflate the lungs of foals 6 months and older, but the curves generated by each method appeared identical. Secondly, FRC, IC and ERV were measured by two independent methods. In the case of FRC, a nitrogen equilibration technique measured an absolute gas volume, while IC and ERV were both derived from measurement of distances on the P-V curves themselves. In order for FRC, ERV, and IC all to be artifactually lower at 3 months of age, several independent errors would have had to have been made, all influencing the results similarly, and this was considered unlikely.

If the first two possibilities are ruled out, the idea that the lungs are growing disproportionately slowly compared to other parts of the body must be considered. There is evidence of this from evaluation of the slopes of allometric equations. The equations of TLC, IC, RV, and FRC were all less than unity, indicating that the lung volumes were increasing at a rate slower than body weight. This concept can perhaps be most easily visualized by examining the pictures of the changing body proportions of the foal over time (Figs. 2-4 to 2-9). At 3 months of age, the foals appeared much taller and stockier than the neonate, with well-developed musculature, but they maintained a very "foal-like" (short-bodied, long-legged) appearance. In the transition from the 3-month-old foal to the adult horse, the trunk and neck must grow, widen, and elongate considerably. It seems reasonable to suggest that as a result of a rapid growth spurt, the 3-month-old foal has increased muscle mass considerably more than he has increased the size of his thorax and thus lungs. This disproportionate growth pattern results in a lower ratio of lung volume/kg in this age group. However, with the development of a longer, wider trunk and a slower rate of growth of the legs, the normalized lung volumes start to increase toward more adult-like proportions, as was seen in the 6 to 12 month old foals.

After the first month of age, the unstressed volume of the chest wall, regardless of whether expressed as a function of BW, TLC, or FRC, decreased significantly with maturation in the foal. At 1 year of age, the absolute 0CW value was only slightly above Vrx (7.12 ± 0.98 L vs 6.3 ± 0.63 L), as can be clearly seen from comparison of the P-V curves in Fig. 2-10. The allometric equation of 0CW supports the same conclusion, as its slope (0.61) is substantially less than that of TLC (0.86), signifying that 0CW increased at a rate slower than TLC as well as body weight (Figs. 2-19 and 2-20). The ratio of FRC/TLC did not appreciably change until the 1 year study period, when it was found to be significantly lower than the values recorded at all the previous study periods up to and including 3 months of age. There are only a few reports documenting the changes in the unstressed volume of the chest wall in other species during growth. Agostoni (1959), in his study of the growing dog, found that 0CW increased from approximately 35% of TLC in the newborn to approximately 60% of TLC in the adult dog. He also found that FRC/TLC increased substantially with growth, from 20.1% in the 1-3 day old puppies to 38.6% in the adult dogs. In another study of several newborn and adult species (Fisher and Mortola, 1980), the results were less consistent. In the rat, both 0CW/TLC and 0CW/kg decreased with age, in the rabbit and cat, 0CW/kg alone was significantly less in the adult, and in the dog, as Agostoni (1959) had reported, both OCW/TLC and OCW/kg were higher in the adult dog. The ratio of FRC/TLC was again significantly higher in the adult dog than the puppy, but was significantly lower in the adult cat than in the kitten. In both studies, a consistent increase in the elastic recoil of the lungs at FRC (PtpFRC) was observed with maturation, as indicated by a more negative Pes in the adult animals.

The resting volume of the chest wall and compliance of both the chest wall and lungs, as well as lung size, all interact to determine the resting postion of the respiratory system. To interpret changes in mechanical parameters such as OCW/TLC and FRC/TLC observed during growth, changes in chest wall compliance must be addressed as well. In almost all studies of chest wall compliance during growth, a consistent finding has been a high C_W at birth which progressively decreases with age. This finding has been reported in the puppy (Agostoni, 1959), goat (Avery and Cook, 1961), rat, rabbit, kitten (Fisher and Mortola, 1980), guinea pig (Gaultier et al., 1984), and human infant (Gerhardt and Bancalari, 1980; Richards and Bachman, 1961), and in the present study, the horse is no exception. During the first 3 months of age, the C_W/kg steadily decreased to approximately 44% of its value in the newborn foal. After that time, there were no further changes observed in that parameter. The difference between the compliance of the newborn and yearling chest wall can be best appreciated by visualization of the P-V curves (Fig. 2-10). Both C_W/C_L and Pw at TLC continued to increase from 3 to 6 months of age, although this was statistically significant only for the Pw value (Table 2-7). The value of C_W/C_L at 1 year of age (0.343) was 35.7% of that at day 2 of life (0.96). Both of these values are considerably lower than those reported for newborns and adults of other species (Mortola, 1983c). It has been well-documented (Leith and Gillespie, 1971) that the adult horse has an extremely stiff chest wall. It appears from the present study that the neonatal foal has a chest wall that is stiffer than that of most other neonates, but not nearly as stiff as that of the adult horse. Therefore, with growth, the foal must still make a transition similar to that of neonates of other species in terms of chest wall compliance. Chest wall compliance/kg reaches the normal adult value at about 3 months of age, but other parameters, such as Pw at TLC, C_W/TLC, and 0CW/TLC continue to change for another few months.

Agostoni (1959) attributed the progressive increase of FRC/TLC he observed during growth in dogs to both a reduction of the compliance of the chest wall and to an increase of 0CW/TLC. He explained the increase in the PtpFRC with age by the increase in FRC due to the decrease in chest wall compliance, as the normalized lung compliance did not change appreciably with growth. From the results of the present study, however, it is clear that the mechanical properties of the respiratory system can mature in different ways in other other species. During the growth process in the foal, PtpFRC and the ratio of FRC/TLC remained constant while both OCW/TLC and C_W/kg decreased. The decreasing chest wall compliance was offset by a downward shift in position of the chest wall curve, as evidenced by the decreasing OCW, which resulted in a constant FRC/TLC and PtpFRC with maturation. It is probable that the term newborn foal's chest wall has sufficient outward elastic recoil to effectively oppose the inward pulmonary elastic recoil and passively maintain end-expiratory lung volume.

Lung compliance increased linearly with body weight and age, and the slope of the allometric equation was close to unity (Table 2-8). When normalized to body weight, the only significant difference over the study period was at 3 months, when a minimum value was reached (Fig. 2-15). The ratio of C_L/kg was also lower at day 2 of age, but not significantly so. As compliance is lung volume dependent and the curves of C_L/kg and TLC or IC/kg vs age looked very similar to one another (Figs. 2-15 and 2-13), the low value at 3 months was attributed to the disproportionate growth of other body structures relative to the lungs, as discussed in the previous section. When normalized to FRC for a measurement of "specific" lung compliance, lung compliance was significantly lower at day 2 of age as well as at 3 months of age. There have been conflicting reports in other neonatal species concerning lung compliance and the changes associated with age. Lung compliance normalized to lung weight in the newborn dog and pig was comparable to the adult value (Agostoni, 1959; Fisher and Mortola, 1980). In the same study (Fisher and Mortola, 1980), a smaller C_L/LW was observed in the neonatal cat, rabbit, and rat, which the authors speculated might be due to incomplete maturation of the alveoli and the relatively greater amount of lung tissue in the newborn (Dunnill, 1962). The C_L/LW was also lower in the newborn human infant (Cook, 1958), guinea pig (Gaultier et al., 1984), and goat (Avery and Cook, 1961) compared to the corresponding adult. As the lungs of the newborn guinea pig (Lechner and Banchero, 1982) and goat (Bartlett and Areson, 1977) are considerably more mature structurally than those of a number of other species such as the rat, it was suggested that increased lung distensibility with age might be due to factors other than tissue proliferation. These include changes in surface forces, surfactant composition, alveolar size, elastin and collagen content and the geometry of alveolar walls (Gaultier et al., 1984). Which if any of these factors might be involved in the maturation of the equine lung is not known at this time.

The total respiratory system compliance, normalized to body weight, fell with increasing postnatal age. This reduction appeared to be influenced mainly by the fall in C_W/kg, as the graphs of the two parameters against age (Fig. 2-16 and 2-17), appeared to be very similarly shaped and the slope of the allometric equation (Table 2-8) of C_W (0.58) was very similar that of C_{RS} (0.65).

Comparison of mechanical parameters in yearling foals to those in adult horses. In the transition from neonate to yearling, the foal undergoes a tremendous change in size and body proportions. However, it is also clear that the yearling still has a considerable amount of growth remaining in order to reach an adult conformation by approximately 3 years of age. The same may be said for the respiratory system as well. Table 2-9 compares the respiratory parameters of the yearling horses measured in this study to those of anesthetized adult horses which were published previously. From examination of this table, it can be seen that several parameters, including C_W/kg, C_L/kg, have reached adult values by 1 year of age. Although IC/kg was slightly lower in the yearling horses, the biggest difference between the 2 groups was seen in the other lung volumes. The values of TLC/kg, RV/kg and FRC/TLC at 1 year of age were still considerably lower than measured in the adults, largely as a result of low FRC values in the yearlings. As this finding was unexpected, it merits some discussion. The discrepency could have resulted from a number of different possibilities, including a disease process or abnormality in the foals, the effect of anesthesia and/or positioning, an error in FRC determination, a dysanaptic growth process, or a methodological error in the adult studies. As stated previously, every attempt was made to insure the health of the foal and its respiratory system prior to each study. All

Table 2-9. Respiratory parameters of yearling horses and previous reports in anesthetized, adult horses.

Variable	Yearling Value (Sternal)	Adult Horse[a] (Sternal)	Adult Horse[b]		
			Sternal	Lateral(R)	Lateral(L)
TLC(L)	21.4	42.1	45.0	37.0	36.0
TLC/kg(ml/kg)	67.9	93.1	92.8	76.3	74.2
IC(L)	15.0	23.2	28.0	25.5	24.5
IC/kg(ml/kg)	47.7	51.3	57.7	52.6	50.5
FRC(L)	6.3	18.9	17.0	11.5	11.5
FRC/kg(ml/kg)	20.1	41.8	35.1	23.7	23.7
ERV(L)	3.7	9.8	8.0	4.5	4.5
ERV/kg(ml/kg)	11.7	21.7	16.5	9.2	9.2
RV(L)	2.7	9.1	9.0	7.0	7.0
RV/kg(ml/kg)	8.5	20.1	18.6	14.4	14.4
FRC/TLC(%)	29.6	44.9	38	34	30
RV/TLC(%)	12.5	21.6	20	19	16
ERV/TLC(%)	17.1	23.3	17.8	12.2	12.5
C_L(L/cmH_2O)	1.41	3.4	1.35	1.37	1.62

Table 2-9. continued

Variable	Yearling Value (Sternal)	Adult Horse[a] (Sternal)	Adult Horse[b]		
			Sternal	Lateral(R)	Lateral(L)
C_L/kg(ml/cmH_2O/kg)	4.5	7.5	2.8	2.8	3.3
C_W(L/cmH_2O)	0.44	0.90	0.78	0.68	0.65
C_W/kg(ml/cmH_2O/kg)	1.41	1.99	1.61	1.40	1.34

[a] Leith and Gillespie (1971).

[b] Sorenson and Robinson (1980).

of the yearlings appeared clinically healthy, were afebrile, and had normal appearing chest radiographs prior to their studies. In addition, all 5 foals studied at 1 year of age were found to follow the same trend. It was therefore considered unlikely that an inherent abnormality in the foals studied resulted in the low lung volumes.

The possibility that positioning and/or anesthesia influenced the lung volume measurements needs to be discussed. It would have been obviously preferable to have obtained all data on the mechanical properties of the respiratory system from the standing, awake, rather than the sternal, anesthetized foal, especially if attempting to draw any conclusions concerning the awake breathing strategy from the results. Unfortunately, measurement techniques that require even the least bit of subject cooperation are extremely difficult in the awake adult horse, and are virtually impossible in the healthy foal. Derksen and co-workers (1980 and 1982) successfully executed quasic-static P-V maneuvers and FRC determinations in standing ponies, but the ponies were heavily sedated and the upper airways were bypassed by the insertion of a cuffed endotracheal tube into a tracheostomy incision. Furthermore, it could not be confirmed that all respiratory muscles were totally relaxed during these awake measurements, although circumstantial evidence suggested that they were. From observation of the behavior of the healthy foal, it was considered unlikely that this sort of procedure would be tolerated at all nor that they would completely relax their respiratory muscles. Functional residual capacity is the only lung volume other than tidal volume that has been measured in full-sized, standing horses (McDonell and Hall, 1974; Gallivan, 1981). The remainder of the reports on the static and dynamic mechanical properties of the lungs and chest wall in the adult horse have been generated in the anesthetized state (Dewes et al., 1974; Mapleson and Weaver, 1969; Purchase, 1966; Sorenson and Robinson, 1980). Therefore, in order to obtain a complete set of data in the immature animal which could be compared in a meaningful way to previous studies in the adult, it was concluded that anesthesia was required.

At least two studies have been conducted to specifically investigate the effect of positioning and anesthesia on respiratory parameters in the adult horse. McDonell and Hall (1974) reported that in the transition between the standing awake horse and the laterally recumbent horse, a 48% reduction in FRC occurred. In an effort to more fully explain that finding, Sorenson and Robinson (1980) performed P-V curves and measured FRC in anesthetized horses placed in 4 different positions: prone, right and left lateral recumbency, and supine. They found that in the transition from prone to lateral recumbency, TLC, FRC, ERV, and RV significantly decreased, while RV/TLC remained the same. Although not a significant difference, the FRC/TLC ratio did decrease from 38% in sternal recumbency to 30% in right lateral recumbency. The authors suggested that the decrease in lung volumes was more a result of position rather than of general anesthesia. However, Gallivan (1981) reported a 34% drop in FRC associated with a transition from a standing, awake to sternal, anesthetized position in a small group of adult horses.

Similar studies have been performed in smaller animals as well, with differing results. In one study (Lai et al., 1979), induction of thiopental anesthesia in the dog had no significant effect on lung volumes or on the pressure-volume relationships of the lungs or chest wall. Contrary to the findings in the horse, in the dog, change in position had little effect on the parameters in either the awake or anesthetized state. In the adult human (Westbrook et al., 1973), rat (Lai and Hildebrandt, 1978), and dog (Avery and Sackner, 1972) muscle paralysis added to anesthesia did not produce any significant changes in respiratory mechanics, suggesting that the respiratory muscles were essentially relaxed at end expiration. However, as it was not known to what extent the respiratory muscles were used during expiration in the anesthetized foal, muscle paralysis was used to insure complete relaxation.

All of the present studies were to be performed in the same body position to avoid the possible variability from this source, and specific studies to examine the effect of body position on respiratory variables in the growing foal were therefore not performed. However, if the results acquired in the adult horse studies are extrapolated to the yearling horse, and studies in the dog are extrapolated to the more similarly sized neonatal foal, a possible explanation for the low lung volumes at 1 year of age emerges. Although every attempt was made to maintain the foals as upright as possible during the studies, as the size of the foals increased, it became increasingly more difficult to maintain this posture. Therefore, most of the older foals were tipped to a modest degree towards lateral recumbency. From Table 2-9, it can be appreciated that the lung volume values in the yearlings most closely approximate the values obtained in the laterally recumbent adults. Therefore, it is possible that positioning did influence our measurements of lung volume and this may at least partially explain the discrepency between yearling and adult values.

Along the same lines, the abdominal contents of the foals may have played an increasingly important role in lung volume determination with growth. During maturation, the equine large colon develops tremendously to occupy a substantial portion of the abdominal cavity, including the area in the concavity created by the dome of the diaphragm. As the foals were not fasted for longer than 12 hours prior to their studies, it is possible that the large colon of the older foals contained a substantial amount of feed material and/or gas. As the ventral abdominal wall contacted the floor in our sternally recumbent foals and was probably pushed upward, it is probable that the abdominal contents were pushed upward and/or forward to some extent as well. If the viscera were filled with ingesta, it is possible that the upward abdominal displacement could have displaced the diaphragm cranially and caused a decrease in lung volumes. As the fasting histories and the exact sternal position utilized in the adult studies are not given, it is difficult to speculate on whether these factors played a role in the differences observed in lung volumes between adult and yearling.

Another possibility that could explain the low FRC values in the older foals is an error associated with the technique utilized to measure FRC. For all studies, a closed-circuit nitrogen equilibration technique was used. This technique was chosen because it could easily be used in the paralyzed, apneic subject, while a number of other techniques require that the animal be spontaneously breathing. Although the addition of muscle paralysis did not produce any significant changes in FRC or in lung elastic properties in anesthetized human subjects (Westbrook et al., 1973), rats (Lai and Hildebrandt, 1978), or dogs (Avery and Sackner, 1972), it was felt preferable to measure FRC under the same conditions that were present when the other lung volumes and compliances were measured. In addition, the reproducibility of the test was very good, and several replications could be performed in a short period of time. A similar method had been previously used for studies of lung volumes in the dog (Robinson et al., 1972) and in the adult horse (Sorenson and Robinson, 1978). In the horse, Sorenson and Robinson (1980) found no significant differences between FRC results determined by this method, by a single-breath N_2 washout, or by a plethysmographic method (Leith and Gillespie, 1971). However, the FRC results acquired in the dog study were higher than had been reported previously using other techniques. The authors listed 2 major sources of potential errors associated with the N_2 equilibration test: nitrogen excretion from body stores and failure to achieve equilibrium during the test. Based on previous calculations for human adults (Rahn et al., 1949), which estimated an error of approximately 0.1 percent due to nitrogen excretion during this type of test, no correction was made for nitrogen excretion in the foal FRC determinations. However, as pointed out in dogs by Simmons and Hemingway (1955), cardiac output/kg BW is about twice as high in the dog as in the human. Since nitrogen excretion is proportional to blood flow, respiratory nitrogen excretion would be expected to be twice as high in the dog as in the human. Robinson et al. (1972) estimated that his FRC measurements could be up to 5% high as a result of error, and the same could be true of the foal measurements. However, this would obviously not contribute to a falsely low FRC.

On the other hand, failure to achieve an equilibrium between alveoli and syringe could account for an artifactually low FRC measurement. However, at each age group studied, an in-line, rapidly responding nitrogen meter was used to monitor the equilibration process on a breath-to-breath basis. In each age group, a minimum nitrogen concentration was observed at the end of either the third or fourth breath. After that time, with each subsequent breath, the measured nitrogen concentration slowly but steadily rose. This same phenomenon was described and analyzed in depth by Rahn and his colleagues (1949). They felt that the increase observed was far too great to be explained by nitrogen excretion. Instead, they felt that a much better explanation was that a decrease in volume occurred secondary to oxygen consumption in a system with a low CO_2 output. During the initial mixing of syringe and alveolar air, P_ACO_2 is reduced to less than half the normal value, so that excess CO_2 leaves the lung. Therefore, the respiratory quotient (R.Q.) should be well above 1.0 initially, but rapidly falls to abnormally low values because CO_2 output becomes very small (due to the large storage capacity of the body for CO_2). The authors calculated that the average R.Q. for the first 3 breaths was very close to 1.0, and the volume change was therefore negligible at that time. Therefore, the authors recommended measurement of nitrogen concentration at the end of the third breath in humans. In the foal studies, from the results of the in-line nitrogen analysis, a total of 4 breaths of volume close to inspiratory capacity were delivered. Progressively increasing the number of breaths delivered from 4 to 15 resulted in steadily increasing FRC measurements in all ages of foals. It is therefore felt that previous studies which utilized a large number of breaths for this type of test may have actually reported falsely elevated FRC values. Although the possibility was not ruled out, a good methodological reason as to why the FRC values in the older foals might have been artifactually too low (outside of positioning) could not be identified.

The possibility that the lower FRC/TLC ratio observed at 1 year of age was really the result of a dysanaptic growth process instead of an artifact of positioning or measurement technique must be considered. Although at first impression an unlikely explanation, it is conceivable to suspect that not only may whole organ systems grow at different rates but certain structural elements of the same organ may also grow out of phase with each other. In a study of the mechanical and structural properties of the growing rat lung, Nardell and Brody (1982) found evidence for such a concept. Postnatal lung development in the rat was divided into 4 stages, each distinguished by specific structural and functional characteristics. The first stage (day 1-4), termed the period of lung expansion, was characterized by low quantities of elastin and collagen, low lung volume/lung weight ratios, low lung elastic recoil, and a high hysteresis ratio. During the period of alveolar proliferation (4-12 days of age), elastin and collagen content increased somewhat, surface area and lung volumes increased, hysteresis ratio decreased, but lung elastic recoil was still low and the lung was easy to rupture. From 12-20 days of age, the third period, alveolar walls thinned considerably, elastin content increased threefold while collagen rose at a much slower rate, elastic recoil pressure doubled, and lung volumes increased by approximately 1.5 times. The lung remained quite easy to rupture. During the final period, elastin content plateaued while collagen content doubled, there was no change in lung volumes/lung weight ratios or other mechanical parameters with the exception that the lung became much less susceptible to rupture. The study was supportive of the idea that increased elastin content was associated with increased elastic recoil while an increased collagen content was associated more closely with enhanced structural integrity. Further, these events occurred at different times in development.

The applicability of the information generated in the rat study to the question of dysanaptic growth in the developing equine lung is unknown, as very little is known about the structural maturity of the equine lung at birth. Although some of the mechanical data suggests that equine lung is probably considerably more mature at birth than the rat lung, there may still be uneven growth of certain elements which could potentially cause a transient change in the interrelationships between lung volumes at 1 year of age. However, as PtpFRC, C_W, C_L, and OCW were all unchanged from previous values at the one year study, in order for that theory to be feasible, additional factors need to be identified that could contribute to a decrease in Vrx or a relative increase in TLC compared to FRC at that age.

The final obvious area in which the P-V curves of the yearling and adult horse seemed to differ considerably was in the behavior of the curves at residual volume. Leith (1976) reported that very low intrathoracic pressures were required (to -60 cm H_2O or lower) in order to reach RV. Thus, in the adult horse, as in the adult human, RV was determined primarily by the stiffness of the chest wall, rather than by airway closure. In the neonatal horse, as stated previously, RV appeared to be set by airway closure. In the yearlings, there was no significant change from the newborn value in the minimum Pes reached at RV, and the shape of the chest wall curves in most of the animals suggested that there was still substantial airway closure at RV. However, the opening pressures required for inflation to TLC from RV did not appear to be as great in the yearlings as in the younger foals (Fig. 2-11). As the foals were not followed past 1 year of age, it was not determined when the lower part of the chest wall curve began to resemble that of the adult horse.

In this study, the static mechanical properties of the respiratory system of a small group of neonatal foals during the first year of life were investigated. It was found that, although certain aspects of the foal's respiratory system differed from those of less mature neonates, particularly in terms of a lower chest wall compliance, a lengthy transition period was still observed until adult values were reached. Characteristics of this transition period included a decrease in C_W/C_L and OCW/TLC ratios, a constant FRC/TLC through out most of the study period (until 1 year of age) and an unchanging PtpFRC. Considerable evidence was found to suggest that the growth of the foal and its respiratory system was in many ways a dysanaptic process. These results suggest that the pattern and time frame of growth of an organ system in an animal relatively mature at birth may differ considerably from those less mature. Therefore, it is unwise to make broad, unqualified extrapolations from studies in one species of neonate and apply them to another.

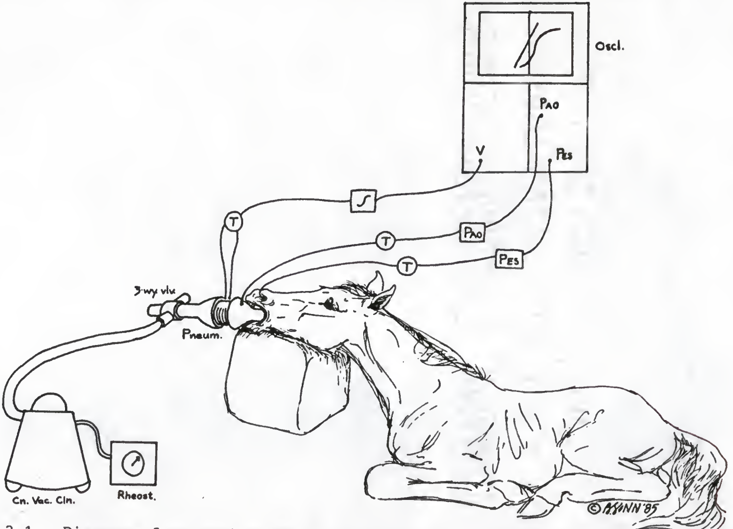


Figure 2-1. Diagram of apparatus used to measure lung volumes and compliance. Pneum., pneumotach; 3-wy. vlv., 3-way valve; Cn. Vac. Cln., air blower used to inflate older foals' lungs; rheos., rheostat to control air blower; T, transducer; ʃ, integrator; Oscl., oscilloscope, where V (volume), Pao, and Pes were displayed for generation of P-V curves.

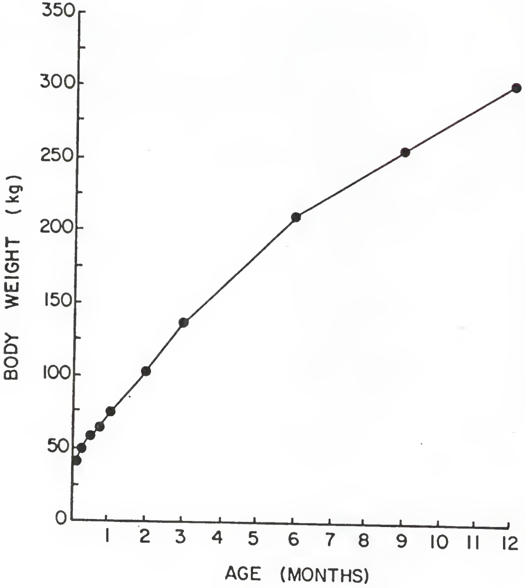


Figure 2-2. Average body weights (kg) of all foals studied from birth to 12 months of age.

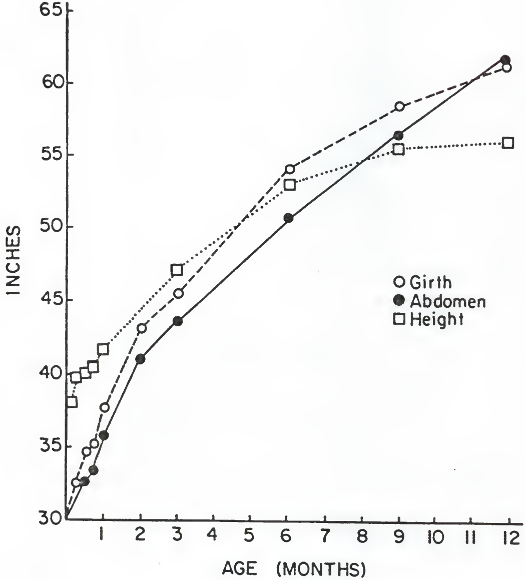


Figure 2-3. Average growth curves for all foals studied showing height at withers, girth, and abdominal circumference measurements from birth to 12 months of age.

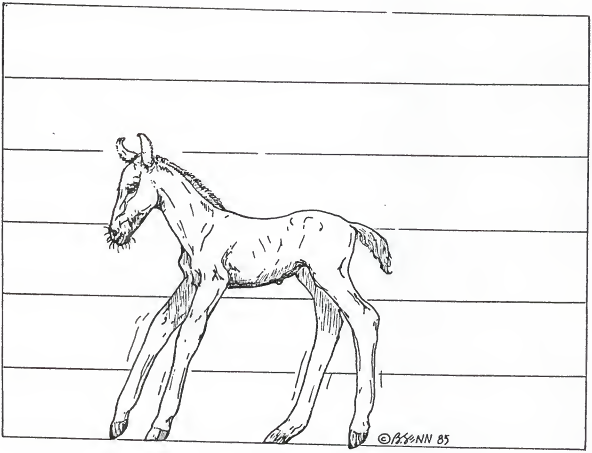


Figure 2-4. Scale drawing of typical 24 hour old Thoroughbred foal. The interval between 2 horizontal lines represents 12 inches.

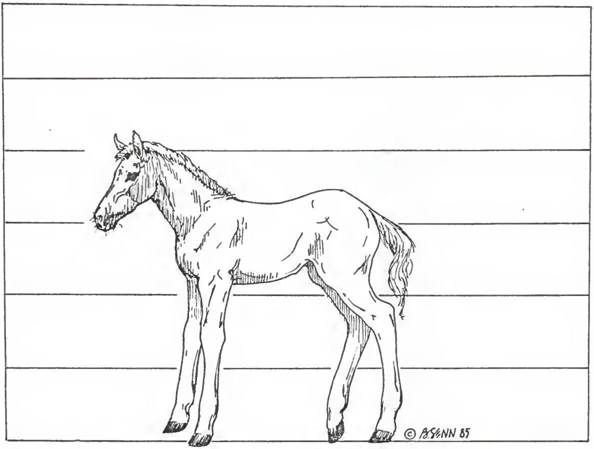


Figure 2-5. Scale drawing of typical 1 month old Thoroughbred foal. The interval between 2 horizontal lines represents 12 inches.

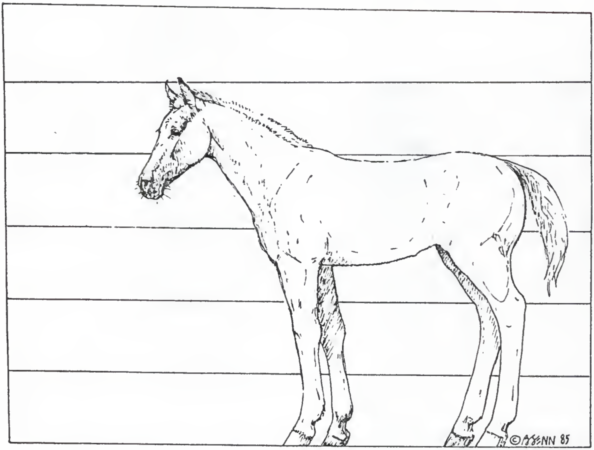


Figure 2-6. Scale drawing of typical 3 month old Thoroughbred foal. The interval between 2 horizontal lines represents 12 inches.

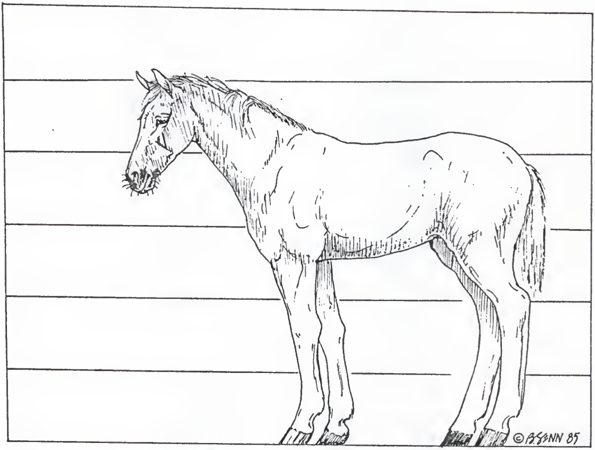


Figure 2-7. Scale drawing of typical 6 month old Thoroughbred foal. The interval between 2 horizontal lines represents 12 inches.

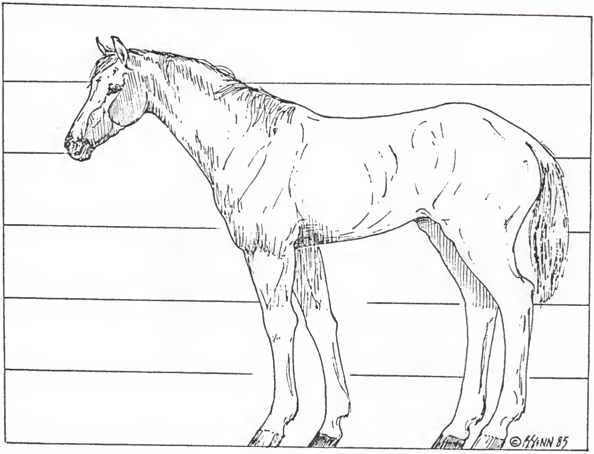


Figure 2-8. Scale drawing of typical 12 month old Thoroughbred foal. The interval between 2 horizontal lines represents 12 inches.

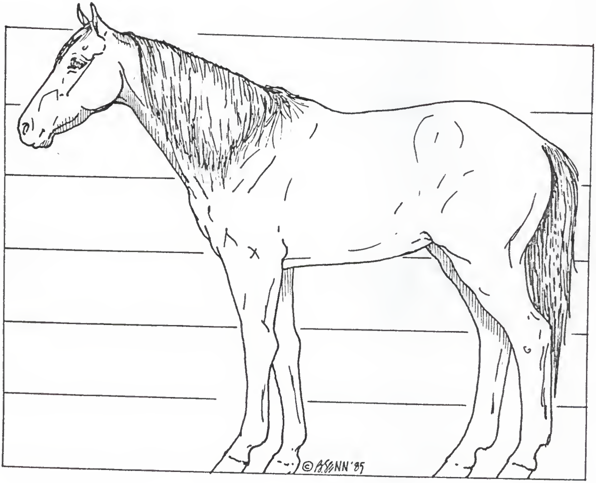
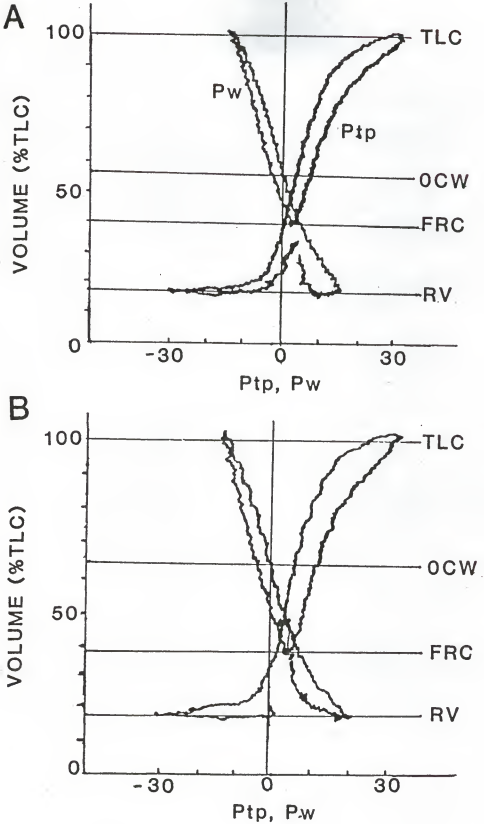


Figure 2-9. Scale drawing of adult horse. The interval between 2 horizontal lines represents 12 inches. Approximate body weight is 450 kg.

Figure 2-10. Quasistatic pressure-volume curves for lung and thorax of representative foals at 24 hours of age (A and B); and at 12 months of age (C and D). The P_W = transthoracic pressure (cmH_2O) and has signs opposite to that illustrated on scale for Ptp (transpulmonary pressure). Also illustrated are major lung volume subdivisions.


A
100
50
0
VOLUME (%TLC)
-30
0
30
Ptp, Pw
TLC
Pw
Ptp
OCW
FRC
RV
B
100
50
0
VOLUME (%TLC)
-30
0
30
Ptp, Pw
TLC
OCW
FRC
RV

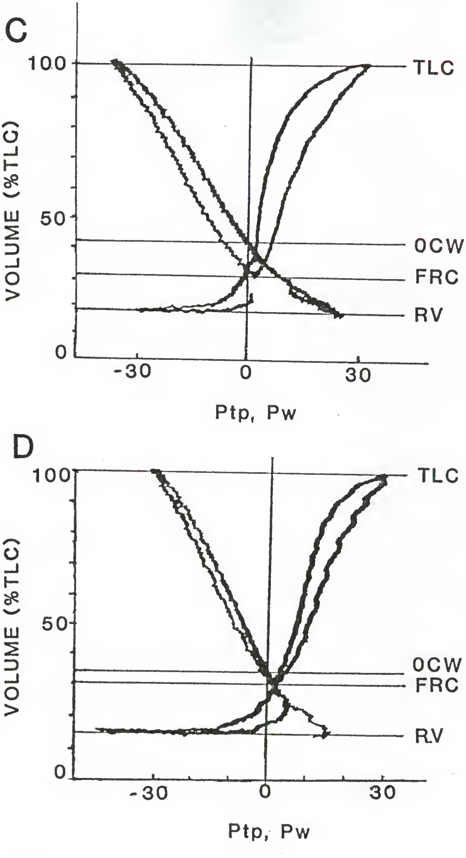


Figure 2-10. Continued.

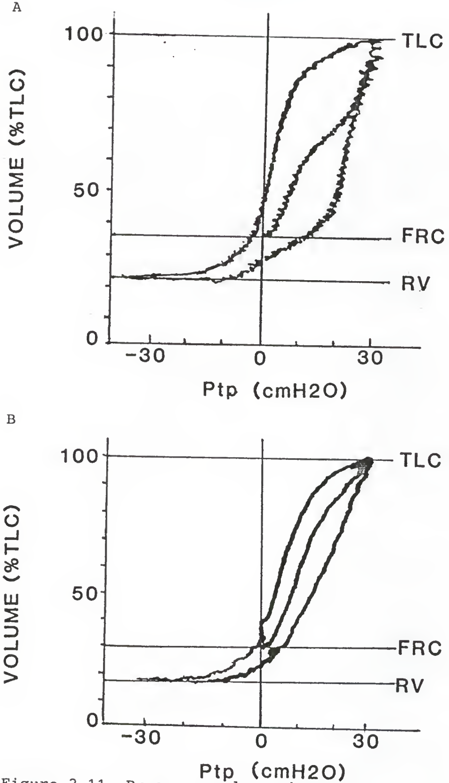


Figure 2-11. Pressure-volume characteristics of lungs during inflation from FRC and RV to TLC. A) Typical curves in a 1 week old foal. Note high opening pressures required for inflation from RV. B) Typical curves in 1 year old foal.

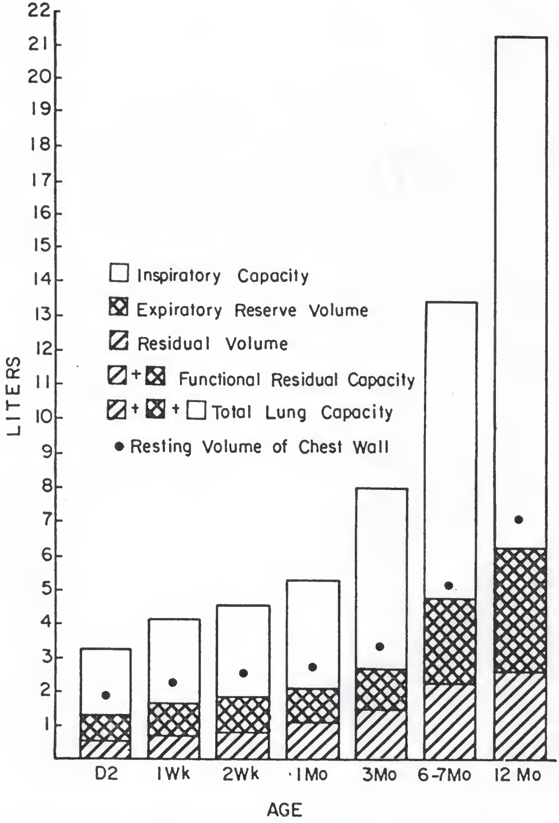


Figure 2-12. Lung volume subdivisions in the growing foal.

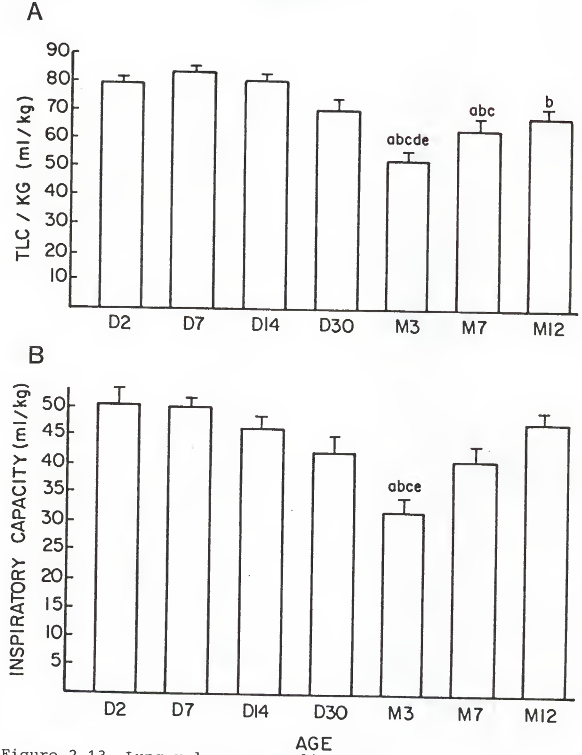


Figure 2-13. Lung volumes normalized to body weight in the foal from day 2 (D2) to 12 months (M12) of age. A) Total lung capacity/kg; B) Inspiratory capacity/kg; C) Functional residual capacity/kg; D) Expiratory reserve volume/kg; E) Residual volume/kg; E) Resting volume of chest wall/kg. Lower case letters denote significant differences as outlined in Table 2-3. Means ± SEM.

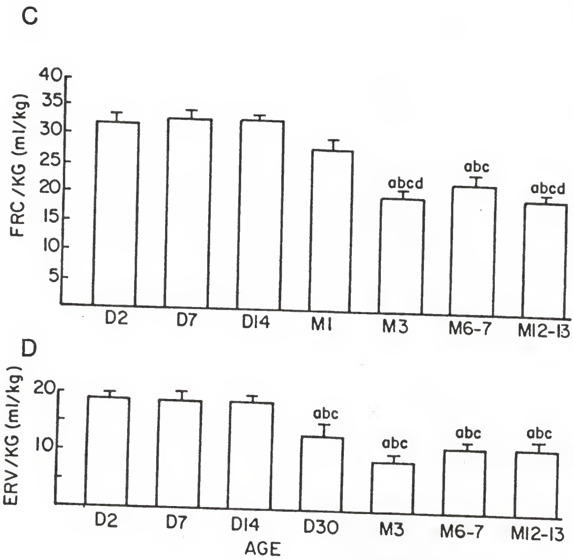


Figure 2-13. Continued.

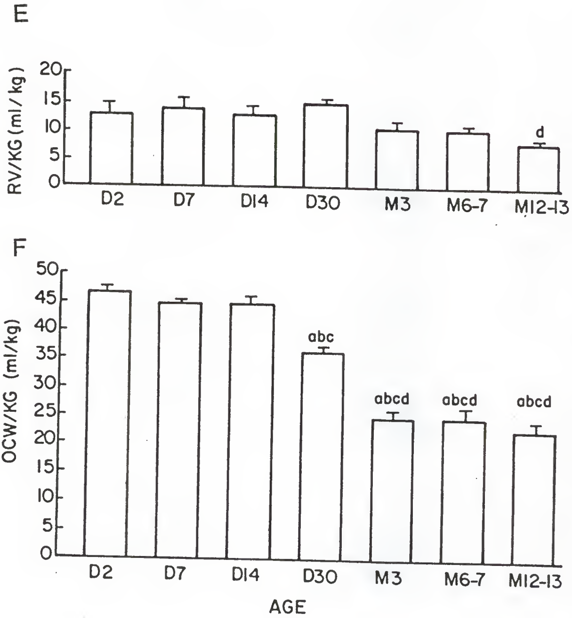


Figure 2-13. Continued.

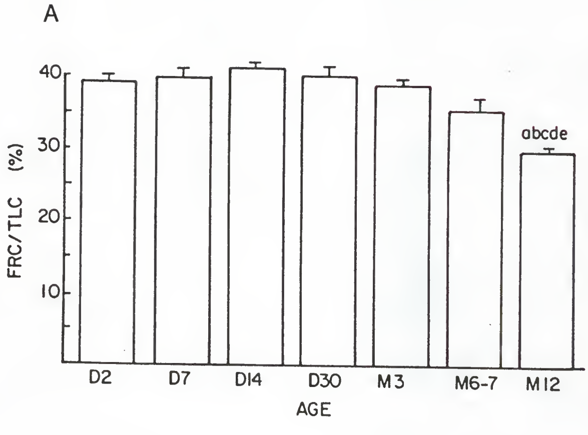


Figure 2-14. Lung volumes as a percent of total lung capacity (TLC) or functional residual capacity (FRC) in the foal from day 2 (D2) to 12 months (M12) of age. A) Functional residual capacity/ TLC; B) Residual volume/TLC; C) Expiratory reserve volume/TLC; E) Resting volume of chest wall/TLC; F) Resting volume of chest wall/FRC. Columns indicate mean values, vertical bars represent standard error (SE).

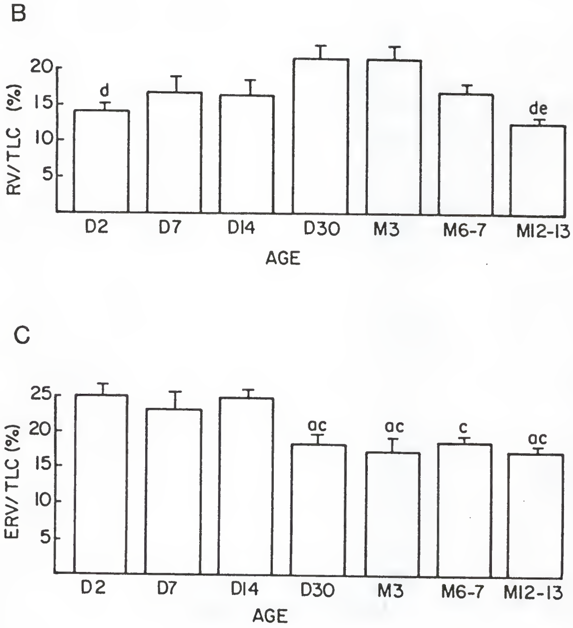


Figure 2-14. Continued.

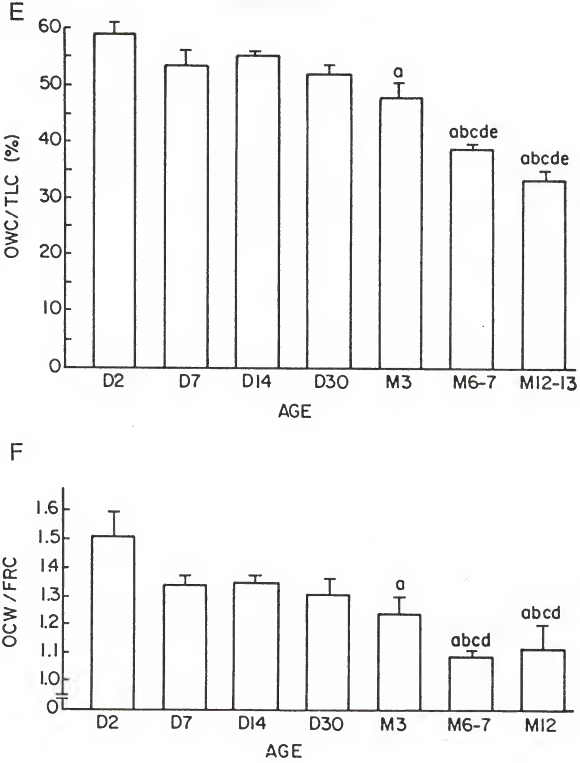


Figure 2-14. Continued.

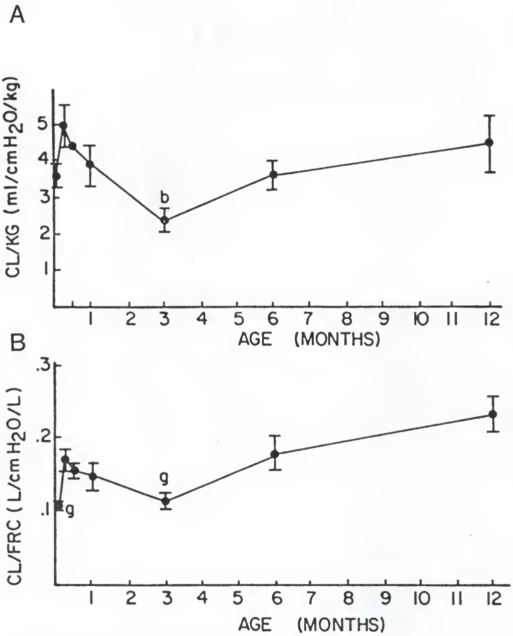


Figure 2-15. Lung compliance in the foal from day 2 to 1 year of age. A) Lung compliance normalized to body weight (kg); B) Lung compliance normalized to functional residual capacity. Solid circles represent mean values, vertical bars represent standard error. Lower case letters indicate significant differences as described in Table 2-6.

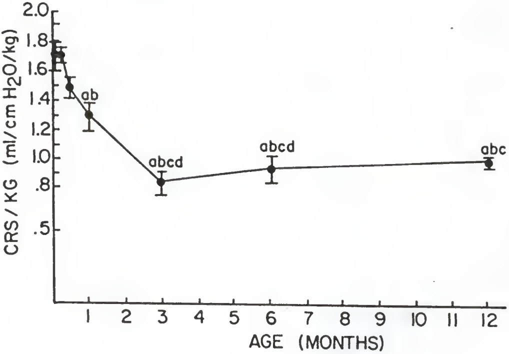
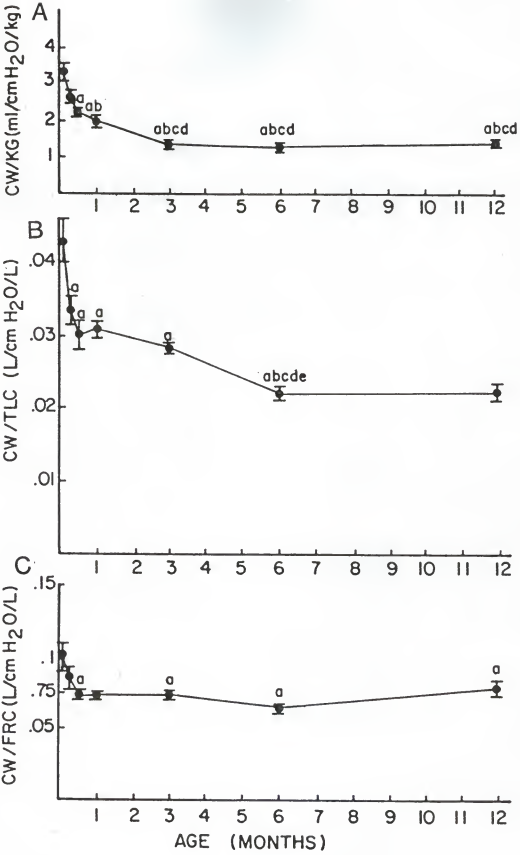


Figure 2-16. Total respiratory system compliance normalized to body weight in the growing foal from day 2 to 12 months of age. Solid circles represent mean values, vertical bars, ± standard error. Lower case letters indicate significant differences as described in Table 2-6.

Figure 2-17. Chest wall compliance in the growing foal from day 2 to 1 year of age. A) Chest wall compliance normalized to body weight (kg); B) Chest wall compliance normalized to total lung capacity (TLC); C) Chest wall compliance normalized to functional residual capacity (FRC). Solid circles represent mean values, vertical bars represent standard error. Lower case letters indicate significant differences as described in Table 2-7.


A
CW/KG (ml/cm H2O/kg)
4
3
2
1
a
ab
abcd
abcd
abcd
1
2
3
4
5
6
7
8
9
10
11
12
B
CW/TLC (L/cm H2O/L)
.04
.03
.02
.01
a
a
a
a
abcde
1
2
3
4
5
6
7
8
9
10
11
12
C
CW/FRC (L/cm H2O/L)
.15
.1
.75
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1
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11
12
AGE (MONTHS)

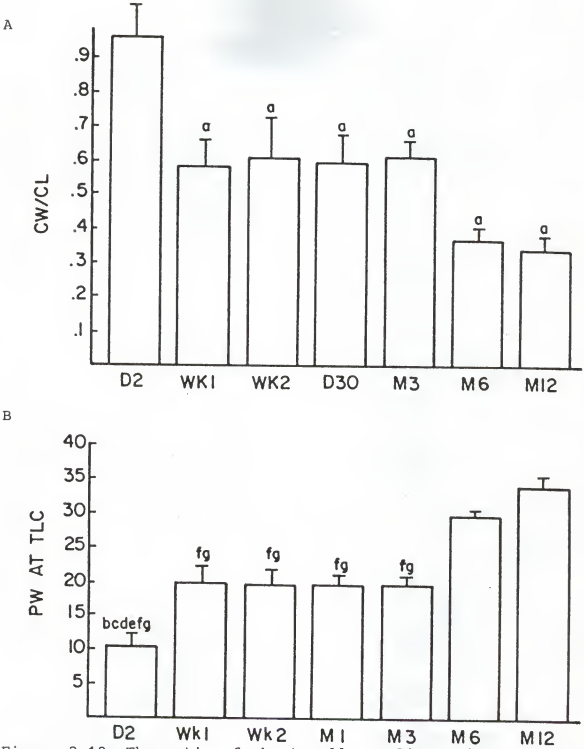


Figure 2-18. The ratio of chest wall compliance to lung compliance (A), and the transthoracic pressure (Pw) at total lung capactiy (B) in the growing foal during the first year of life. Columns indicate mean values, vertical bars denote standard error. Lower case letters denote significant differences as described in Table 2-7.

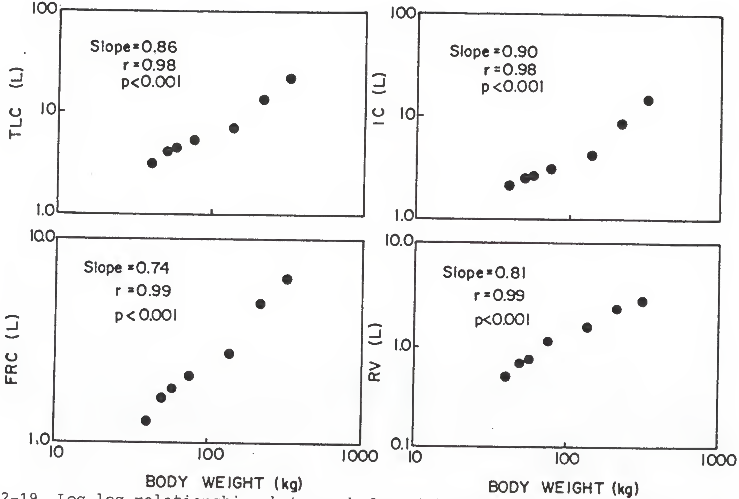


Figure 2-19. Log-log relationships between body weight (kg) and lung volumes in the growing foal during the first year of life. Upper left panel) Allometry of total lung capacity; Upper right panel) Allometry of inspiratory capacity; Lower left panel) Allometry of functional residual capacity; Lower right panel) Allometry of residual volume.

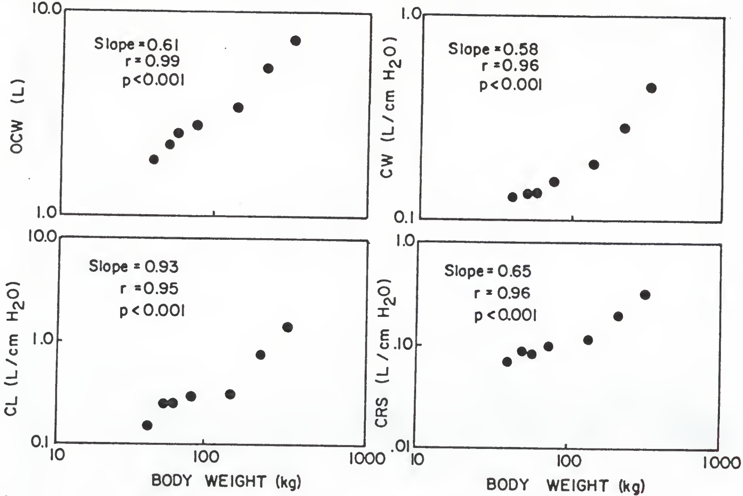


Figure 2-20. Log-log relationships between body weight (kg) and lung volume and compliance in the growing foal during the first year of life. Upper left panel) Allometry of the resting volume of the chest wall; Upper right panel) Allometry of chest wall compliance; Lower left panel) Allometry of lung compliance; Lower right panel) Allometry of total respiratory system compliance.

CHAPTER III
BREATHING STRATEGY OF THE FOAL FROM 24 HOURS TO ONE YEAR OF AGE

Introduction

Two major determinants influencing the strategy of breathing utilized by a particular species are its metabolic requirements and the mechanical characteristics of its respiratory system (Mortola, 1984). As both of these factors are different in the newborn than in the adult, it might be expected that the neonatal breathing pattern would differ as well. A general characteristic of the newborn animal is a considerably higher metabolic rate (normalized to body weight) compared to the adult of the same species, which necessitates a high ventilation. Minute ventilation may be increased by increasing the frequency of breathing, by an increase in tidal volume or by a combination of the two, but there are mechanical disadvantages associated with each of these. An increase in tidal volume increases the elastic work of breathing, and an increase in respiratory rate increases the resistive work of breathing and may also require marked repiratory muscle activity to move sufficient air in the short time period available (Mortola, 1983a and 1984).

The mechanical characteristics of the chest wall of the neonate may also play an important role in determining the breathing pattern adopted. A high chest wall to lung compliance ratio relative to the adult is a consistent finding in all species of neonates studied to date (Agostoni, 1959; Avery and Cook, 1961; Fisher and Mortola, 1980; Gaultier et al., 1984; Mortola, 1983c). Although probably necessary for an uncomplicated delivery through the birth canal, the flexibility of the chest wall may adversely affect both gas exchange and the efficiency of ventilation in a number of ways. First, if tidal volume is increased, chest wall distortion would be expected to increase during inspiration due to an inadequate support of the contracting diaphragm (Mortola, 1983c; Mortola et al., 1982). Second, as the relaxation volume of the respiratory system (Vrx) is determined by a balance between the tendency of the lungs to recoil inward and the tendency of the relaxed chest wall to recoil outward, a high chest wall compliance (lower outward elastic recoil) would be expected to predispose to a low Vrx. A low Vrx could be disadvantageous to the neonate in several ways. At end-expiration, the alveoli and small airways would be smaller and have a greater tendency to collapse, and the work of the respiratory muscles would have to be increased in order to reinflate the closed units. Second, the lack of a sizable gas reservoir at end-expiration would predispose to decreased O_2 stores (Findley et al., 1983) and oscillations in alveolar gas composition resulting in alterations in blood gas concentration. Apneic episodes, as are commonly observed in the preterm and term human newborn, would be expected to be poorly tolerated in a system with a low Vrx.

There is, however, a considerable body of evidence which suggests that unanesthetized newborns of several species, including the human infant, do not deflate to Vrx at end-expiration but rather actively maintain end-expiratory lung volume (EEV) well above Vrx. This may be accomplished by several different mechanisms. In a system with a high chest wall compliance, the passive time constant, the product of resistance and compliance, should be prolonged. As a result, the expiratory time required for passive emptying of the lungs to Vrx would be increased. A rapid breathing rate with a short expiratory time (T_E) could elevate EEV above Vrx by reducing the time available for complete emptying of the lungs. Olinsky et al. (1974) suggested that this strategy was utilized by the human neonate when they observed in a preterm infant a decrease in EEV associated with spontaneous unobstructed apneas. They postulated that the fall in lung volume during these pauses was due simply to sufficient time being available for deflation to Vrx. However, in studies of the breathing pattern of several species of anesthetized (Griffiths et al., 1983; Mortola, 1983a) and awake newborns (Mortola, 1984), it was calculated that at normal breathing frequencies in most species, this mechanism alone could only account for a small fraction of the difference between EEV and Vrx observed. It was postulated that as the frequency of breathing increased either in very small species such as the rat and mouse, or in disease states, that this strategy could play a more important role.

Two additional strategies potentially useful in maintaining an elevated EEV are post-inspiratory inspiratory muscle activity and upper airway narrowing during expiration. Both mechanisms exert the same effect on the system; that is, retard or brake expiratory airflow. The former strategy decreases the rate of lung deflation by counteracting the passive recoil of the respiratory system towards the relaxation volume, while the latter increases expiratory resistance to airflow. In animals (Bartlett et al., 1973; Farber, 1978; Gautier et al., 1973; Harding et al., 1980) and human infants (Radvanyi-Bouvet et al., 1982), spontaneous airflow retardation during expiration has been shown to decrease the rate of lung deflation as well as cause a reflex prolongation of T_E. Although a longer T_E could allow passive deflation to a volume closer to Vrx, the more important effect of airflow braking in the human neonate appears to lie in its mechanical effect in maintaining lung volume (Kosch et al., 1985). Post-inspiratory inspiratory muscle activity has been well documented in both diaphragm and intercostal muscles of the newborn (Bartlett et al., 1973; Gautier et al., 1973; Kosch and Stark, 1984; Lopes et al., 1981; Remmers and Bartlett, 1977). In adults, during inspiration, the posterior cricoarytenoid muscle abducts the glottis, increasing the airway diameter and reducing resistance, but during expiration in most adult animals, there is little intrinsic laryngeal adductor activity. However, in certain awake newborn animals, including the lamb (Harding et al., 1980), the opossum (Farber, 1978), and puppy (England et al., 1985) laryngeal adductors are active during expiration. In human infants, interruptions of expiratory flow were frequently observed during the first hours after birth, and upper airway closure was suggested as the most likely mechanism for this phenomenon (Fisher et al., 1982). Recently, laryngeal muscle activity has been correlated with specific braking patterns of expiratory flow observed in the normal term human infant (Kosch et al., 1985b). In conclusion, in the newborn species studied previously, it appears that a number of strategies are utilized to defend end-expiratory lung volume in a compliant respiratory system.

There are very few reports of the breathing strategies utilized by neonatal species larger than the human infant. Harding et al. (1980) reported the breathing patterns associated with activities of upper airway and other respiratory muscles in fetal and newborn lambs during sleep and wakefulness and concluded that that the larynx was an important organ of respiration during both inspiration and expiration in this neonatal species. Although Gillespie (1975) speculated that the foal has a respiratory system similar to that of other neonates and thus would be expected to adopt similar strategies to maintain EEV, no evidence in support of this has been published. It would certainly seem disadvantageous to the foal to breathe with the adult horse polyphasic pattern involving active deflation to an EEV substantially less than Vrx. From preliminary studies of the breathing pattern of neonatal pony foals and from one report illustrating airflow tracings against time in two young (5 and 6 months old) horses (Amoroso et al., 1963) it appeared that both inspiration and expiration in the foal were monophasic, and the pattern more closely resembled a typical neonatal breathing pattern than one of an adult horse. No electromyographic (EMG) or pressure measurements were made, however, to confirm that the foals were breathing above or from Vrx.

The purpose of the present study was twofold. First, the hypothesis that the awake, quietly breathing foal, a considerably larger neonate than previously studied, uses breathing strategies similar to those utilized by neonates of smaller species to defend lung volume, was tested. In addition, the changes in ventilatory parameters and breathing strategy during the first year of life were followed, in an attempt to better understand both the adult horse's strategy of breathing and the changes in respiratory function associated with growth. In particular, the time course of change in breathing strategy was compared with the time course of change in the mechanical properties of the lungs and chest wall (Chapter II) in order to specifically assess the influence of a stiffening chest wall on breathing strategy.

Materials and Methods

Ten horse foals born over a two year period at the College of Veterinary Medicine, University of Florida were utilized for the awake breathing studies. Information concerning the gestational ages and birth weights of the individuals studied may be found in Table 2-1 of the preceding chapter, and other details concerning the foals may be found in the text of the Materials and Methods section of that chapter. The ages at which awake breathing studies were performed were similar to those of the static mechanics studies, except that the foals in the present study were also studied awake at 3 weeks, 2 and 9 months of age. As in the previous study, foals #1 - 5 were serially studied during the first year of age, while foals #6 - 10 were studied only during their first month of age. All foals were maintained in a pasture with their mothers until 5-6 months of age when they were weaned and housed together in a smaller paddock. Assessment of the normalcy of the foals' respiratory system was determined prior to each study as described in Chapter II.

Prior to each study, the unrestrained foal's respiratory rate and breathing pattern was observed from a distance in an attempt to assess the influence of the study conditions on the measured parameters. The mares were subsequently sedated and the foals were removed from the mothers to an enclosed air conditioned room where the studies were conducted. Ambient temperature in the study room averaged 75-80°F year round, while the outside temperature varied considerably from around 50°F in the winter to frequently well over 90°F during the summer months. All foals were studied in a fully padded enclosure within the large room, with at least 2 people acting as restrainers to keep the animals in proper position (Fig. 3-1). Because the young foals were considerably more cooperative in lateral compared to the standing position, all foals one month of age or less were placed in lateral recumbency for instrumentation. Foals older than one month remained standing during the procedure. No tranquilization was utilized in any of the studies until 3 months of age, when a low dose of xylazine (Rompun, Haver-Lockhart; 0.15-0.25 mg/kg intravenously) was generally required for smooth introduction and proper placement of the esophageal and gastric balloons. In the studies in which sedation was utilized, the airflow pattern was measured with the pneumotach system prior to administration of the tranquilizer. In addition, measurements were generally not made until the foals appeared free from the behavioral effects of the drug, usually 30 to 45 minutes following injection. In several foals, when it was necessary to repeat certain measurements on a second study day in order to acquire complete data on the desired respiratory parameters, the results from the two studies were averaged.

For measurement of airflow ($\dot{V}$), tidal volume (Vt), and airway pressure (Pao), a fiberglass facemask holding one Fleisch No. 4 pneumotachograph was utilized. As in the adult version, a band of rubber innertube material cemented to the fiberglass was secured to the foal's head with electrical tape to form an airtight seal (Figure 3-2). One of three different sized masks were used, depending on the size of the foal and the muzzle conformation, in order to obtain the best fit possible and reduce dead space to a minimum. The dead space of the smallest mask, used during the first month of life, was 75-100 ml, while the dead space of the largest one, used in foals 6 months of age and older, was somewhat greater. A ± 5 cmH_2O differential pressure transducer (Validyne model MP-45) was used to measure the pressure drop across the pneumotachograph and this signal was electronically integrated to yield volume (Validyne integrator model FV-156). The system was calibrated as described in Chapter I. The Pao was measured with a ± 2 cmH_2O differential pressure transducer from the proximal port of the pneumotach.

Esophageal (Pes) and gastric (Pga) pressures were measured with 7-8 cm long, thin-walled, hand-dipped latex balloons sealed over the end of Teflon PFA tubing (Cole Palmer Instrument Co.; internal diameter 2 mm, and 200 cm long) that had a number of perforations in the tubing underlying the balloon. Each catheter was connected via a 3-way stopcock to the positive side of a ± 50 cmH_2O

differential pressure transducer, with the negative side open to the atmosphere. Both Pga and Pes balloons were routinely filled with 2 ml of air during the studies. The frequency responses of the balloon-catheter systems were tested using the method of Jackson and Vinegar (1979). A flat response in amplitude was observed to over 10 Hz, and in phase to over 4 Hz. This response was considered adequate for measurement of respiratory parameters in the foal at rest. All pressure transducers were calibrated using a water manometer system.

Intercostal (Eint) and abdominal (Eabd) EMGs were recorded from paired surface electrodes (Sylvan ECG electrode, NDM Corp.) positioned over the 11th or 12th intercostal space at mid-thoracic level, and over the lower flank area, respectively (Figure 3-3). The EMG signals were amplified (Coulbourn Instruments model S75-04B), connected via a fiber optic cable to a fiber optic receiver (Coulbourn Instruments model S75-04), and recorded on an 8-channel FM tape recorder (Vetter model D). In the young foals, due to the thinness of the intercostal muscles and activity of the foals, it was very difficult to percutaneously place and maintain the type of fine wire intramuscular electrodes used in the adult horse studies. The surface electrodes were much easier to place and maintain as long as the skin was properly prepared. This preparation included shaving of the hair, rubbing the skin with alcohol, and sealing the electrodes to the skin with osteostomy cement. In a few of the older foals, fine wire electrodes were successfully utilized to obtain recordings of Eint activity.

The EMG signal from the diaphragm (Edi) was measured using the same type of intraesophageal electrode system described in Chapter I. However, for use in the foals, the inter-electrode distance was shortened to 2.0 cm. (Fig. 3-4), and the overall length of the tubing was shortened to 200 cm. The Edi signal was bandpass filtered between 100 and 3000 Hz with attenuation slopes of 3dB/octave by the differential amplifier (Tektronix model AM502).

In foals less than 6 months of age, the balloon-catheter systems were passed into the esophagus through a flexible silastic modified endotracheal tube (Fig. 3-5; Bivona Surgical; 55 cm long, 8 mm internal diameter). Because of the relatively small size of the young foals' nasal passages, a tube of this approximate size was required, but associated with it was the disadvantage of only being large enough to pass through it two balloon-catheters. Thus, a combination of only two of the three parameters (Pes, Pga, Edi) could be measured at any one time in the younger foals. After the catheters were advanced to the stomach or caudal esophagus, and the position of the balloons were confirmed by observation of the pressure tracings or Edi signal on a storage oscilloscope (Tektronix model 5113), the silastic tube was removed. The catheters were then taped securely to the foal's head, the facemask was applied and recording was begun. In the foals 6 months of age and older, all three balloon-catheters were passed into the stomach in a well-lubricated adult horse nasogastric tube as described in Chapter I.

All signals were recorded on the FM tape recorder during periods of quiet breathing, and observations of the behavior of the foal at the time of the recording were noted on a voice track. In foals less than 1 month of age, following instrumentation, the foals were maintained in lateral recumbency, and recordings of breathing strategy were made. The majority of the foals relaxed considerably during this time, and several appeared to enter rapid-eye-movement (REM) sleep, judging from behavioral criteria such as muscle twitching and leg and eye movements. The time of transition to sleep was noted on the voice channel for later correlation with breathing pattern. The foals were subsequently assisted to their feet and all measurements were repeated with the foal standing quietly. Because of their size, foals over one month of age were studied in the standing position only.

Ventilatory parameters, mechanical timing intervals, and pressure changes were determined by computer analysis (Digital Equipment model PDP-11/23). Depending on the study, the number of breaths analyzed in each position ranged from 10 to 50. Airflow, tidal volume, and airway, esophageal and gastric pressures were digitized at a sampling rate of 200 Hz and the digitized data were displayed on a graphical terminal (Tektronix model 4010-1). Mechanical inspiratory (T_I) and expiratory (T_E) times were determined from the zero crossover points on the flow tracings. Tidal volume was measured from the volume tracing. The ratio of T_I:T_E, total breath duration (T_{TOT}), T_I:T_{TOT}, instantaneous breathing frequency ($1/T_{TOT}$ X 60), and minute ventilation ($\dot{V}_E$; $1/T_{TOT}$ X 60 X Vt) were calculated breath-by-breath and averaged. Airflow measurements were made in several ways. The average inspiratory and expiratory flow rates ($\dot{V}$meanI, $\dot{V}$meanE) were calculated from the digitized flow tracings, and mean inspiratory flow was obtained by division of Vt by T_I. All values were expressed in both absolute terms and as functions of body weight. When inspiration and/or expiration were biphasic, the two peaks of flow ($\dot{V}$peak1 and $\dot{V}$peak2) and the intervening low point in flow ($\dot{V}$dip) were measured as well. In addition, the times within each inspiration and/or expiration when the peaks and dips in airflow occurred were determined and were expressed in both seconds and as a percentage of T_I or T_E. In addition to computer analysis, $\dot{V}$ and Vt signals were displayed on an X-Y storage oscilloscope and flow-volume loops for individual breaths were photographed with a Polaroid camera.

For calculation of dynamic compliance (Cdyn), Vt was divided by the difference in esophageal pressure at the two points of zero airflow. Total pulmonary resistance (Rpul) was determined by both an isovolume method (Marshall, 1965) and by the subtraction technique (Neergaard and Wirz, 1927) described in Chapter I for measurement of both inspiratory and expiratory pulmonary resistance. As no substantial differences were observed between the values obtained using the two techniques, only the results from the isovolume computations are reported. The maximum change in Pes between expiration and inspiration (ΔPesmax), and the maximal change observed in Pga (ΔPgamax) during both inspiration and expiration, were measured and recorded. Transdiaphragmatic pressure (Pdi) was determined by continuous subtraction of Pga from Pes and was displayed on the graphics terminal along with the other pressure tracings. The Pdi tracings generated were visually inspected in order to describe the changes in Pdi associated with expiration and early inspiration. In addition, the time interval between the onset of inspiratory flow and a decrease or change in downward slope of Pdi was determined.

For EMG analysis, taped data was replayed onto a 6-channel pen writer (Gould model 260) and storage oscilloscope. Surface EMG recordings were routinely high-pass filtered at 100 Hz (Rockland model 452) which effectively reduced the often prominent motion and cardiac artifacts commonly associated with surface recordings. Representative airflow and EMG tracings plotted against time and against volume at each age group were displayed on the oscilloscope and photographed with a Polaroid camera. For each study, the overall pattern of respiratory muscle activation was observed. The presence or absence of persistent intercostal muscle and diaphragm activity into expiration was recorded. In addition, the time intervals between onset of inspiratory flow and onset of both Edi and Eint were recorded for each breath and averaged. The same comparison was made between onset of expiratory flow and Eabd. In selected breaths, the raw Eabd, Edi or Eint signal was electrically added to the flow signal and plotted against volume on the oscilloscope for generation of "paintbrush" flow-volume loops.

As only short segments of quiet, regular breathing were selected for computer and EMG analysis, there was concern that the segments analyzed did not accurately reflect the overall breathing strategy of the foal. Therefore, in addition to the analysis outlined above, much longer strip-chart recordings of the breathing parameters were scrutinized in an attempt to form more meaningful conclusions concerning the range and relative incidences of the breathing patterns utilized by the growing foal.

In each foal, beginning at 1-2 weeks of age and repeated at approximately 2 month intervals, respiratory inductance plethysmography (RIP) was utilized, as in the adult horses (Chapter I), to examine the effect of the facemask on the resting breathing pattern of the foal. With the exception of the use of human adult respibands instead of the large animal bands, the studies in foals were carried out in the same manner as described in Chapter I for the adult horses.

Statistical Analysis

For each study, ventilatory, timing, and pressure parameters for individual breaths were averaged and standard deviations were calculated to obtain mean values for individual foals in each study. The averaged data for each foal were subsequently averaged with all other foals studied at that age group. In order for more meaningful comparisons to be made between foals of different sizes and ages, certain ventilatory parameters such as Vt, $\dot{V}_E$, average inspiratory and expiratory flow rates, Cdyn and Rpul were normalized to body weight. In order to test the effect of increasing age on breathing pattern, two-way analysis of variance and Tukey's Studentized Range test for multiple comparisons were performed by the computer to compare selected respiratory variables obtained at each of the 10 age groups. Only data acquired in the standing position were used for these comparisons. A statistically significant difference between two age groups was defined by $P < 0.05$ for a two-tailed t test. Linear regression analyses were also performed using age as the independent variable and the respiratory parameters as dependent variables. In addition, Vt, $\dot{V}_E$, f, Cdyn, and Rpul were transformed to base 10 logs for least squares regression analyses of allometric equations of the form $y = ax^b$, as described in Chapter II. The values of the correlation coefficients (r) and the differences of the slopes were tested for significance for a two-tailed t test. The Student t test was used for comparision of values obtained in foals at one week and one year of age to those obtained in the group of adult horses in Chapter I. Finally, in foals one month of age and less, a paired t test was used to compare variables obtained in the awake foal in lateral recumbency to those obtained in the standing animal.

Results

Ventilatory and Timing Parameters in the Standing Foal During Growth

Table 3-1 shows the average body weights and ventilatory parameters of Vt, Vt/kg, f, $\dot{V}_E$, and $\dot{V}_E$/kg for each age group studied and the results of the multiple comparison tests. In Table 3-2 are regression equations relating the same parameters to age, and in Figure 3-6 the plots of the parameters are graphically represented. Tidal volume and minute ventilation both increased linearly with age ($P < 0.001$). However, when normalized to body weight, Vt/kg remained relatively constant through the first year of life, with the exception that at 3 weeks and from 2 to 6 months of age, Vt/kg was significantly lower than the value recorded at day 7 of age (Table 3-1). At 2 months, Vt/kg reached a minimum value of 9.8 ml/kg. Breathing frequency decreased thoughout the first year of age, and although the regression equation fit a linear model, from examination of the plot (Fig. 3-6), it can be appreciated that the pattern of decline more closely resembled a curvilinear function. As f decreased substantially with age while only small changes

Table 3-1. Ventilatory parameters in standing foals in first year of life.

Age	n	BW (kg)	V_T (L)	V_T/kg (ml/kg)	f (breaths/min)	$\dot{V}_E$ (L/min)	$\dot{V}_E$/kg (ml/min/kg)
Day 2	7	40.8	0.646 ±0.147	15.8 ±2.5	53.9 ±9.9	34.8 ±12.0	848 ±231
Week 1	9	46.1	0.798 ±0.173	17.6 ±3.0	40.9^{a} ±5.16	33.9 ±7.5	717 ±157
Week 2	6	58.1	0.823 ±0.080	14.3 ±1.9	37.6^{a} ±10.7	30.1 ±6.5	523^{a} ±126
Week 3	6	63.7	0.802 ±0.101	11.3^{b} ±5.6	37.7^{a} ±9.6	30.7 ±11.2	436^{ab} ±259
Month 1	8	74.8	0.978 ±0.124	13.1 ±1.6	34.1^{a} ±10.6	32.4 ±8.5	436^{ab} ±116
Month 2	6	104.8	1.10 ±0.34	9.8^{ab} ±2.6	32.1^{a} ±7.7	32.5 ±6.1	300^{ab} ±42
Month 3	5	136.6	1.45 ±0.19	10.7^{b} ±1.9	26.9^{ab} ±5.7	37.7 ±3.9	277^{ab} ±42
Month 6	6	210.2	2.38 ±0.31	11.7^{b} ±1.1	15.8^{abcdef} ±1.5	38.9 ±4.1	171^{abc} ±42

Table 3-1. continued

Age	n	BW (kg)	V_T (L)	V_T/kg (ml/kg)	f (breaths/min)	$\dot{V}_E$ (L/min)	$\dot{V}_E$/kg (ml/min/kg)
Month 9	5	256.2	3.28 ±0.22	12.8 ±1.2	14.8^{abcdef} ±3.8	46.9 ±11.1	183^{abc} ±34
Year 1	5	303.6	3.88 ±0.50	12.8 ±1.4	$12.5^{abcdefg}$ ±2.0	47.0 ±4.1	155^{abcef} ±15

means ± SD

V_T = tidal volume, f = frequency of breathing, $\dot{V}_E$ = minute ventilation, BW = body weight. a = value is significantly less than that at day 2; b = value is significantly less than that recorded on day 7; c = value is significantly less than that on day 14; d = value is significantly less than that on day 21; e = value is significantly less than that recorded on day 30; f = value is significantly less than that on day 60.

Table 3-2. Linear regression equations for means of respiratory variables and body weight as a function of age in growing foals.

Parameter	Slope	Intercept	Correlation Coefficient (R)	P Value Slope $\neq 0$
V_T (L)	0.009	.661	0.998	<0.0001
V_T/kg (ml/kg)	-0.005	13.7	0.321	0.183
f (breaths/min)	-0.094	40.6	0.89	0.0003
$\dot{V}_E$ (L/min)	0.046	31.7	0.94	<0.0001
$\dot{V}_E$/kg (ml/min/kg)	-0.0015	562.6	0.77	0.005
V_T/T_I (L/sec)	0.003	1.11	0.94	<0.0001
ave. insp. $\dot{V}$ (L/min)	0.135	60.6	0.92	<0.0001
ave. exp. $\dot{V}$ (L/min)	0.052	54.8	0.91	0.00014
T_I (sec)	0.004	0.726	0.97	<0.0001
T_E (sec)	0.007	0.754	0.99	<0.0001
T_{TOT} (sec)	0.011	1.48	0.99	<0.0001
T_I/T_E	-0.0008	0.93	0.87	0.0006
$T_I \Delta P_{di}$ (sec)	0.0011	0.011	0.72	0.0096

Table 3-2. continued

Parameter	Slope	Intercept	Correlation Coefficient (R)	P Value Slope $\neq 0$
ΔP_{esmax} (cmH_2O)	0.006	14.35	0.19	0.302
ΔP_{gamaxI}	0.003	1.90	0.52	0.062
ΔP_{gamaxE}	0.009	3.58	0.81	0.002
C_{dyn} (L/cmH_2O)	0.0015	0.108	0.99	<0.0001
C_{dyn}/kg ($ml/cmH_2O/kg$)	-0.0014	2.35	0.31	0.188
R_{pul} ($cmH_2O/L/min$)	-0.00006	0.068	0.27	0.224
R_{pul}/kg ($cmH_2O/L/min/kg$)	0.0000	0.0011	0.78	0.004
RC (sec)	0.003	0.56	0.72	0.01
Body weight (kg)	0.749	52.2	0.99	<0.0001

V_T = tidal volume; f = frequency; $\dot{V}_E$ = minute ventilation; T_I = inspiratory time; T_E = expiratory time; $\dot{V}$ = flow; $T_I \Delta P_{di}$ = time in inspiration when P_{di} begins to decrease; ΔP_{esmax} = change in esophageal pressure during inspiration; ΔP_{gaI} and ΔP_{gaE} refer to changes in gastric pressure during inspiratiory and expiration; C_{dyn} = dynamic compliance; R_{pul} = total pulmonary resistance.

in Vt/kg were noted, the product of the two, $\dot{V}_E$/kg, also significantly decreased with growth in a pattern paralleling the decrease in f (Fig. 3-6). Similar conclusions may be drawn from the allometric equations for Vt, f, and $\dot{V}_E$ which are listed in Table 3-3 and illustrated in Fig. 3-7. The negative slope of the equation for f indicated that breathing rate decreased in progressively larger foals, and as the slope for Vt was slightly less than unity, Vt was increasing at a somewhat slower rate than body weight. The slope of the line for $\dot{V}_E$ (the product of f and Vt) was therefore considerably less than unity (0.19). In comparison to the adult values (Table 3-4), Vt/kg was slightly, but significantly, lower in the yearlings, while both f and $\dot{V}_E$/kg were very similar in the two groups.

The values for average inspiratory and expiratory airflow ($\dot{V}_{meanI}$ and $\dot{V}_{meanE}$), obtained using the flow tracing, and mean inspiratory airflow, Vt/T_I, were expressed in both absolute terms and as functions of body weight and are presented in Table 3-5. The relationship of $\dot{V}_{meanI}$/kg to age is illustrated in Fig. 3-8. As expected, when normalized to the same units of airflow measurement, the values for Vt/T_I and $\dot{V}_{meanI}$ closely paralleled one another. Both were significantly lower during the first 2 months than at 9 and 12 months of age (Table 3-5). However, when normalized to body weight, both parameters decreased significantly with age until 6 months of age, after which no further changes were observed (Table 3-5 and Fig. 3-8). Although mean

Table 3-3. Allometric equations for means of respiratory variables during awake breathing in growing foals.

Parameter	Slope (b)	Intercept (a)	Correlation Coefficient (r)	P Value for b ≠ 0
V_T (L)	0.865	0.022	0.98	<0.0001
f (breaths/min)	-0.662	602	0.99	<0.0001
$\dot{V}_E$ (L/min)	0.187	15.1	0.84	0.00011
C_{dyn} (L/cmH$_2$O)	0.93	.003	0.97	<0.0001
R_{pul} (cmH$_2$O/L/min)	-0.13	0.110	0.22	.29

V_T = tidal volume; f = frequency; $\dot{V}_E$ = minute ventilation; C_{dyn} = dynamic compliance; R_{pul} = total pulmonary resistance.

Table 3-4. Ventilatory, timing, and pressure values in neonatal and yearling compared to adult values.

Parameter	1 Week Old Foal	Yearling	Adult
Body weight (kg)	46.1 ± 5.8	303 ± 10.9	474.44
V_T (L)	0.80 ± .17**	3.88 ± .50**	6.84 ± 1.29
V_T/kg (ml/kg)	17.4 ± 2.9*	12.8 ± 1.4*	14.3 ± 2.32
f (breaths/min)	43.1 ± 8.3**	12.5 ± 2.0	10.9 ± 4.2
$\dot{V}_E$ (L/min)	33.9 ± 7.5**	47.0 ± 4.1*	76.8 ± 21.2
$\dot{V}_E$/kg (ml/min/kg)	744.0 ± 168.5**	154.5 ± 14.4	162.0 ± 44.7
V_T/T_I (L/sec)	1.16 ± 0.22	1.99 ± 0.28	2.84 ± 0.73
T_I (sec)	0.69 ± 0.10**	1.99 ± 0.26	2.48 ± 0.74
T_E (sec)	0.75 ± 0.17**	3.12 ± 0.66	3.37 ± 1.69
T_{TOT} (sec)	1.45 ± 0.24**	5.1 ± 0.86	5.86 ± 2.31
T_I/T_E	0.96 ± 0.16	0.67 ± 0.12	0.83 ± 0.24
ΔP_{esmax} (cmH_2O)	6.65 ± 3.04	6.42 ± 1.76	6.95 ± 1.73

Table 3-4. continued

Parameter	1 Week Old Foal	Yearling	Adult
ΔP_{gaImax} (cmH_2O)	1.90 ± 1.11	3.12 ± 1.88	2.37 ± 1.05
ΔP_{gaEmax} (cmH_2O)	3.46 ± 0.795	7.82 ± 1.98*	4.42 ± 1.41
C_{dyn} (L/cmH_2O)	0.149 ± 0.049*	0.696 ± 0.168*	2.65 ± 1.51
C_{dyn} ($ml/cmH_2O/kg$)	3.28 ± 1.10	2.30 ± 0.62	5.51 ± 3.0
R_{pul} ($cmH_2O/L/min$)	0.05 ± .028*	0.026 ± 0.009*	0.013 ± 0.008

means ± SD

$*P < 0.05$

$**P < 0.001$ --value significantly different than adult value.

V_T = tidal volume; f = frequency; $\dot{V}_E$ = minute ventilation; T_I = inspiratory time; T_E = expiratory time; $\dot{V}$ = flow; P_{esmax} = change in esophageal pressure during inspiration; ΔP_{gaI} and ΔP_{gaE} refer to changes in gastric pressure during inspiratiory and expiration; C_{dyn} = dynamic compliance; R_{pul} = total pulmonary resistance.

Table 3.5. Airflow parameters in standing foals during the first year of age.

Age	V_T/T_I (L/sec)	V_T/T_I x 60/kg (L/min/kg)	$\dot{V}_{meanI}$ (L/min)	$\dot{V}_{meanI}$/kg (L/min/kg)	$\dot{V}_{meanE}$ (L/min)	$\dot{V}_{meanE}$/kg (L/min/kg)
Day 2	1.37±0.61^{j}	2.01±0.90	73.9±33.0	1.80±0.68	56.2±14.6	1.38±0.27
Week 1	1.14±0.23^{ij}	1.48±0.30	60.6±5.70^{ij}	1.33±0.20	55.3±12.2	1.22±0.34
Week 2	1.03±0.23^{ij}	1.06±0.24	57.2±13.9^{ij}	1.00±0.26^{a}	52.8±10.2	0.92±0.20^{a}
Week 3	1.07±0.46^{ij}	1.01±0.43	60.1±24.1^{ij}	0.85±0.52^{a}	53.2±16.4	0.73±0.42^{ab}
Month 1	1.15±0.33^{ij}	0.92±0.26	63.6±17.9^{ij}	0.85±0.21^{a}	57.0±15.4	0.76±0.22^{ab}
Month 2	1.12±0.24^{ij}	0.64±0.14	57.2±15.9^{ij}	0.55±0.11^{ab}	55.4±8.0	0.53±0.08^{ab}
Month 3	1.40±0.23	0.61±0.10	78.9±12.7	0.59±0.13^{ab}	63.8±8.5	0.47±0.07^{abc}
Month 6	1.56±0.39	0.45±0.11	80.6±23.6	0.37±0.12^{abc}	57.0±10.1	0.26±0.08^{abcde}
Month 9	1.95±0.58	0.46±0.14	104.5±34.7	0.40±0.10^{ab}	73.1±15.2	0.29±0.05^{abcde}
Year 1	1.99±0.28	0.39±0.06	106.2±10.3	0.35±0.03^{abc}	71.1±7.5	0.23±0.03^{abcde}
means ± SD					NS	

V_T = tidal volume; $\dot{V}_{mean}$=average inspiratory flow; T_I = inspiratory time; NS = no significant differences. a = value is significantly less than that at day 2; b = value is significantly less than that recorded on day 7; c = value is significantly less than that on day 14; d = value is significantly less than that on day 21; e = value is significantly less than that recorded on day 30; f = value is significantly less than that on day 60; g = value is significantly less than that on day 90; h = value is significantly less than that at 6 mo. of age; i = value is significantly less than that recorded on month 9; j = value is significantly less than that recorded at 1 year of age. Values for n = those in Table 3-1.

expiratory flow also increased in foals 9 months and older, no significant differences were noted using the multiple comparison test (Table 3-5). However, from the regression analyses, all three flow parameters, Vt/T_I, $\dot{V}_{meanI}$, and $\dot{V}_{meanE}$, were found to increase linearly with age (Table 3-2). When $\dot{V}_{meanE}$ was normalized to body weight, a trend similar to that of $\dot{V}_{meanI}/kg$ was observed with maturation.

From Tables 3-2 and 3-6, it is apparent that the prolongation of T_{TOT} with increasing age in the standing foals was the result of an increase in both T_I and T_E. However, prolongation of T_I and T_E during growth was not proportional (Fig. 3-9; Tables 3-2 and 3-6). Inspiratory time increased with age at a slower rate than T_E, resulting in significantly lower T_I/T_{TOT} and T_I/T_E ratios in the foals 6 months of age or older compared to the foals one month of age or less. The same variability observed in individual T_I/T_E ratios in the adult horses (Table 1-2) was observed in individual foals as well, in that the T_I/T_E ratios did not all decrease with age to the same extent in all the foals. Overall, both T_I/T_{TOT}, the respiratory duty cycle (Table 3-6), and $Vt/T_I/kg$, the normalized mean inspiratory flow (Table 3-5) decreased with age, which resulted in a significantly lower $Vt/T_{TOT}/kg$, the normalized instantaneous minute ventilation, according to the equation: $Vt/T_{TOT} = Vt/T_I \times T_I/T_{TOT}$. At one year of age, timing parameters were not significantly different from adult values (Table 3-4).

Table 3-6. Overall timing parameters in foals during the first year of age.

Age	T_I (sec)	T_E (sec)	T_{TOT} (sec)	T_I/T_E	T_I/T_{TOT}
Day 2	0.51^{eghij} ±0.15	0.65^{hij} ±0.10	1.16^{ghij} ±.24	0.79 ±.15	0.44 ±0.05
Week 1	0.72^{hij} ±.09	0.75^{hij} ±.17	1.45^{hij} ±.24	0.94 ±.15	0.48 ±0.04
Week 2	0.84^{hij} ±.27	0.90^{hij} ±0.34	1.75^{hij} ±0.60	0.97 ±0.18	0.49 ±0.05
Week 3	0.82^{hij} ±.20	0.87^{hij} ±.25	1.69^{hij} ±0.44	0.97 ±0.16	0.49 ±0.04
Month 1	0.94^{hij} ±0.34	1.06^{hij} ±0.53	2.01^{hij} ±.85	0.93 ±0.20	0.48 ±0.05
Month 2	0.93^{hij} ±0.19	1.13^{hij} ±0.32	2.09^{hij} ±0.49	0.90 ±0.14	0.47 ±0.04
Month 3	1.08^{hij} ±0.27	1.31^{hij} ±0.32	2.39^{hij} ±0.55	0.84 ±0.14	0.45 ±0.04
Month 6	1.70 ±0.23	2.30 ±0.57	3.92 ±0.70	0.73^{bcde} ±0.17	0.41^{bcdef} ±0.06

Table 3-6. continued

Age	T_I (sec)	T_E (sec)	T_{TOT} (sec)	T_I/T_E	T_I/T_{TOT}
Month 9	1.84 $\pm$0.57	2.76 $\pm$0.80	4.60 $\pm$1.33	0.70^{bcdef} $\pm$0.12	0.41^{bcdef} $\pm$0.04
Year 1	1.99 $\pm$0.26	3.12 $\pm$0.66	5.10 $\pm$0.86	0.67^{bcdef} $\pm$0.12	0.40^{bcdef} $\pm$0.04

means $\pm$ SD

T_I = inspiratory time; T_E = expiratory time; $T_{TOT} = T_I + T_E$. a = value is significantly less than that at day 2; b = value is significantly less than that recorded on day 7; c = value is significantly less than that on day 14; d = value is significantly less than that on day 21; e = value is significantly less than that recorded on day 30; f = value is significantly less than that on day 60; g = value is significantly less than that on day 90; h = value is significantly less than that at 6 mo. of age; i = value is significantly less than that recorded on month 9; j = value is significantly less than that recorded at 1 year of age. Values for n are the same as listed in Table 3-1.

Maturational Changes in Breathing Pattern in the Standing Foal

Tables 3-7 and 3-8 list the maximum and minimum flow rates for inspiration and expiration, respectively, as well as the times at which these events occurred in the respiratory cycle. Although averaged inspiratory and expiratory airflow data can be useful in comparing monophasic breathing patterns, the validity of comparisons of average flows betweeen monophasic and polyphasic patterns is questionable. In addition, when inspiration has both an active and passive component, use of Vt/T_I as an estimate of central inspiratory drive is not appropriate. Overall, with age, the difference between peak flows and the intervening low point in flow during both inspiration and expiration tended to increase. In other words, both inspiration and expiration became more biphasic in character as the foals got older. Although some degree of biphasic expiratory flow pattern was detectable in many of the foals from the first week of age, a biphasic inspiratory flow pattern was not consistently observed until the one year studies. From birth to 9 months of age, the inspiratory airflow and timing values had a large standard deviation and seemed to make very little sense, and they were therefore deleted from Table 3-7. These numbers resulted from the computer identifying small undulations in the inspiratory flow tracing as peaks and low points in flow and indicated that a biphasic flow was not a consistent feature at these ages. On the other hand, during expiration, the computer was able to

Table 3-7. Minimum and maximum inspiratory air flow rates and times during inspiration at which they occur.

Age	T_I (sec)	$\dot{V}_{Ipeak1}$ (L/min)	T_{Ipeak1} (sec)	$\%T_I$	$\dot{V}_{dip}$ (L/min)	T_{Idip} (sec)	$\%T_I$	$\dot{V}_{Ipeak2}$ (L/min)	T_{Ipeak2} (sec)	$\%T_I$
Day 2	0.53	* *	* *	* *	* *	* *	* *	81.6^{ij} ±20.6	0.422 ±0.146	74.7 ±4.8
Week 1	0.69	* *	* *	* *	* *	* *	* *	74.3^{ij} ±7.5	0.492 ±0.91	70.2 ±5.3
Week 2	0.85	* *	* *	* *	* *	* *	* *	70.6^{hij} ±15.7	0.593 ±.210	69.6 ±6.0
Week 3	0.82	* *	* *	* *	* *	* *	* *	69.3^{hij} ±23.7	0.600 ±.144	73.2 ±2.3
Week 4	0.94	* *	* *	* *	* *	* *	* *	79.2^{ij} ±23.1	0.716 ±.301	74.3 ±5.8
Month 2	0.96	* *	* *	* *	* *	* *	* *	68.1^{hij} ±17.6	0.697 ±.161	71.4 ±7.8
Month 3	1.08	* *	* *	* *	* *	* *	* *	94.3^{ij} ±16.1	0.911 ±.38	75.0 ±12.0
Month 6	1.63	* *	* *	* *	* *	* *	* *	103.3^{j} ±15.5	1.34 ±.235	80.6 ±3.8

Table 3-7. continued

Age	T_I (sec)	$\dot{V}_{Ipeak1}$ (L/min)	T_{Ipeak1} (sec)	$\%T_I$	$\dot{V}_{dip}$ (L/min)	T_{Idip} (sec)	$\%T_I$	$\dot{V}_{Ipeak2}$ (L/min)	T_{Ipeak2} (sec)	$\%T_I$
Month 9	1.84	* *	* *	* *	* *	* *	* *	132.2 ±35.5	1.374 ±.475	79.6 ±7.8
Month 12	1.99	138.5 ±18.0	0.387 ±.072	19.8 ±3.9	75.2 ±19.5	0.862 ±.121	43.9 ±3.4	137.6 ±8.7	1.577 ±0.199	79.0 ±3.9

Values are means ± SD

T_I = inspiratory time, $\dot{V}_{Ipeak1}$, $\dot{V}_{Idip}$, and $\dot{V}_{Ipeak2}$ are the first peak, low point, and second peak of inspiratory flow, respectively. T_{Ipeak1}, T_{Idip}, and T_{Ipeak2} refer to time at which each of these events occurs. $\%T_I$ = each of these 3 times divided by T_I; h = value is significantly less than that at 6 mo. of age; i = value is significantly less than that recorded on month 9; j = value is significantly less than that recorded at 1 year of age.

*Denotes deleted data, due to inability of computer to detect the 1st peak and low point in inspiratory flow.

Values for n are the same as listed in Table 3-1.

Table 3-8. Minimum and maximum expiratory air flow rates and times during expriation at which they occur.

Age	T_E	$\dot{V}_{Epeak1}$	T_{Epeak1}	$\%T_E$	$\dot{V}_{dip}$	T_{Edip}	$\%T_E$	$\dot{V}_{Epeak2}$	T_{Epeak2}	$\%T_E$
Day 2	0.65 ±0.10	88.8^{j} ±19.6	0.10 ±0.02	15.5 ±2.4	44.2 ±17.0	0.45 ±0.09	69.3 ±6.5	49.6^{ij} ±19.6	0.49 ±0.08	74.9 ±14.2
Week 1	0.75 ±0.17	89.9^{j} ±21.8	0.12 ±0.03	16.3 ±4.8	42.3 ±9.0	0.47 ±0.10	62.5 ±7.4	51.2^{ij} ±10.9	0.55 ±.14	72.0^{ij} ±6.6
Week 2	0.90 ±0.34	78.0^{j} ±18.0	0.13 ±.02	16.3 ±4.7	43.5 ±11.7	0.49 ±.14	56.9 ±14.5	55.0^{ij} ±11.5	0.67 ±.23	74.8^{i} ±4.9
Week 3	0.87 ±0.25	75.3^{ij} ±24.6	0.13 ±.02	15.9 ±3.2	46.3 ±15.2	0.48 ±.06	58.2 ±12.5	55.8^{ij} ±11.8	0.64 ±0.17	73.6^{i} ±2.1
Week 4	1.06 ±0.53	82.4^{j} ±22.7	0.15 ±.04	15.8 ±6.7	46.7 ±17.0	0.54 ±.13	55.6 ±11.4	63.3 ±13.6	0.79 ±.43	73.2 ±5.4
Month 2	1.13 ±0.32	78.4^{j} ±10.4	0.20 ±.05	18.9 ±8.3	48.4 ±8.3	0.65 ±.19	62.2 ±7.9	55.7^{ij} ±13.0	0.81 ±.24	71.7^{ij} ±1.7
Month 3	1.31 ±0.32	89.0^{j} ±15.3	0.18 ±.04	14.6 ±4.2	50.6 ±13.1	0.71 ±.25	53.6 ±11.4	73.9 ±20.0	1.04 ±0.28	78.9 ±3.3
Month 6	2.30 ±0.57	94.3^{j} ±12.1	0.30 ±.091	12.9 ±4.3	38.0 ±9.2	1.20 ±.45	53.3 ±7.6	63.6 ±22.6	1.79 ±0.44	77.8 ±2.6

Table 3-8. continued

Age	T_E	$\dot{V}_{Epeak1}$	T_{Epeak1}	$\%T_E$	$\dot{V}_{dip}$	T_{Edip}	$\%T_E$	$\dot{V}_{Epeak2}$	T_{Epeak2}	$\%T_E$
Month 9	2.76 ±0.80	114.2 ±33.4	0.29 ±0.06	11.7^f ±2.3	50.0 ±8.8	1.33 ±.38	49.9^a ±4.9	89.3 ±23.9	2.28 ±0.68	81.9 ±5.8
Month 12	3.12 ±0.66	134.4 ±14.0	0.28 ±.03	9.9^f ±3.4	35.9 ±9.3	1.48 ±.28	48.2^a ±2.8	89.3 ±10.2	2.52 ±.59	80.0 ±3.3
					NS					

NS = not significant

T_E = expiratory time; $\dot{V}_{Epeak1}$, $\dot{V}_{Edip}$, and $\dot{V}_{Epeak2}$ are the first peak, low point, and second peak of expiratory flow; T_{Epeak1}, T_{Edip}, and T_{Epeak2} refer to the time at which each of these events occurs during expiration. $\%T_E$ = each of these times divided by T_I. i = value is significantly less than that recorded on month 9; j = value is significantly less than that recorded at 1 year of age.

Values for n are same as listed in Table 3-1.

detect the peaks and low point in flow more accurately and precisely. With increasing age, there was a tendency for both $\dot{V}_{Epeak1}$ and $\dot{V}_{dip}$ to occur at an earlier point in expiration (Table 3-8). Expressed as a percent of T_E, both T_{Epeak1} and T_{Edip} were significantly shorter at 9 and 12 months than at month 2, and day 2, respectively.

A composite breath for the yearling foals, constructed by plotting the mean values of airflow and timing parameters, is shown in Fig. 3-10. If this breath is compared to the adult horse composite breath illustrated in Fig. 1-4, a striking resemblance can be appreciated. With the exception of consistently lower peak flow rates in the foals, the configuration of the two breaths were remarkably similar, suggesting that by one year of age, the foals for the most part had acquired an adult airflow pattern. To aid visualization of the changes that occurred in the character of the breathing pattern over time, Fig. 3-11 shows representative flow-volume loops from 2 of the 5 foals studied over the one-year time period. The flow-volume loops of these 2 foals were representative of the typical patterns observed in the other foals studied. In the younger foals, there was considerable variation in the pattern of expiratory flow, both between foals of the same age and to a lesser extent, within the same foal on different study days, ranging from a monophasic to a more pronounced biphasic pattern. For example, from the first study day on, foal #1 consistently displayed some degree of biphasic expiratory flow pattern, while the flow-volume loops of foal #3 were consistently of a much more box-like configuration, showing little evidence of a biphasic expiratory pattern until approximately 3 months of age (Fig 3-11, panel G). From 3 months of age to 1 year, all foals displayed an obvious biphasic expiratory flow pattern. Although foals 6 months of age and older sporadically showed some evidence of a biphasic inspiratory flow pattern (Fig. 3-11, panels H, I, and J), there was a predominance of an essentially monophasic inspiratory flow pattern until the one year studies (Fig. 3-11, panel J).

Abdominal, intercostal and diaphragm EMG activities were consistently recorded from all standing foals at all ages studied. Table 3-9 lists average differences between onset of EMG activity of the three respiratory muscles and onset of inspiratory or expiratory airflow for each age group of foals studied. The average onset of Edi activity preceded the onset of inspiratory flow, although by a progressively smaller margin, until 1 year of age, when the average time of onset of Edi lagged the onset of inspiratory flow. Examples of the immature pattern of Edi activation are shown in tracings obtained from two 6-day-old foals (Fig. 3-12) and a more mature pattern with marked delays in onset of Edi, obtained from a yearling foal, is shown in Fig. 3-13. Although no foal less than 6 months of age was found to have a consistent delay in Edi activation during awake

Table 3-9. Timing parameters in the normal foal during the first year of age.

	Difference:* Onset of T_I vs $T_{I(Edi)}$ (sec)	Difference:* Onset of T_I vs $T_{I(Eint)}$ (sec)	Difference:* Onset of T_E vs $T_{E(Eabd)}$ (sec)	
			(sec)	($\%T_E$)
Day 2	+0.056 ± .016	+0.012 ± .033	-0.036 ± .034	5.54
Day 7	+0.051 ± .026	+0.015 ± .039	-0.147 ± .074	19.4
Day 14	+0.071 ± .032	+0.015 ± .054	-0.067 ± .095	7.4
Day 21	+0.059 ± .02	-0.034 ± .068	-0.117 ± .075	13.50
Day 30	+0.032 ± .064	-0.021 ± .067	-0.198 ± .115	18.6
2 months	NR	+0.05 ± .055	-0.326 ± .152	28.9
3 months	NR	+0.010 ± .080	-0.410 ± .127	31.2
6 months	+0.020 ± .110	+0.046 ± .134	-1.178 ± .279	50.8
9 months	+0.007 ± .143	-0.194 ± .29	-1.45 ± .266	52.5
12 months	-0.196 ± .27	-0.240 ± .287	-1.43 ± .416	45.8

means ± SD

*Minus sign denotes that onset of EMG activity lags mechanical event (i.e., beginning of inspiratory or expiratory flow). Plus sign denotes that onset of EMG precedes mechanical event.

T_I = inspiratory time, T_E = expiratory time, $T_{TOT} = T_I + T_E$, NR = not recorded.
Values for n: Day 2=6; day 7=8; day 14=5; day 21=6; day 30=6; month 2=5; month 3=4; month 6=5; month 9= 5; month 12=5.

breathing, a delay in Edi was noted in some of the analyzed breaths of foal #8 during her one month study. She also displayed a more adult-like breathing pattern than the other foals studied at that age (Fig. 3-14). There was a slight delay in Edi noted in one of the 5 foals studied at 6 months, in 2 foals at 9 months of age, and a more pronounced delay in 4 of the 5 foals studied at one year of age. It may also be noted in Fig. 3-12 that there is little post-inspiratory Edi activity in either tracing of the one week old foals. While only observed sporadically in the younger foals, in all foals 9 months of age or older, an Edi signal persisting into expiration was observed in the majority of breaths analyzed (Fig 3-13).

Onset of inspiratory Eint activity relative to onset of flow showed a trend with increasing age similar to, but not exactly the same as that of Edi activity (Table 3-9). In the younger standing foals, the mean time of onset of Eint did not appear to precede inspiratory flow by as sizable margin as did Edi activity, and by 9 months of age, a substantial delay in onset of Eint was noted. Persistent Eint activity into the first part of expiration was observed more frequently than persistent Edi activity in all age groups after the first week of age. Post-inspiratory activity was often pronounced as illustrated in tracings from a 2 week and 7 month old foal (Fig. 3-15, A and B). Although this pattern of inspiratory Eint activity, with onset of activity closely associated with the onset of airflow and substantial post-inspiratory activity, was the most common pattern observed, in certain foals and at certain age groups, expiratory intercostal activity was also detected. Appearance of expiratory Eint activity showed little obvious association with age. For example, in foal #1, both expiratory and inspiratory Eint activity were recorded from surface electrodes at day 7, month 9 and month 12 of age, in foal #2 at 5 of the 10 ages studied, and at only one study time in foals #3 and #4. Two examples of the typical Eint activation pattern associated with expiratory Eint activity are shown in Figs. 3-16 and 3-17. These tracings were recorded using both surface (Fig. 3-16) and fine wire (Fig. 3-17) electrodes. Expiratory Eint activity was most commonly observed during the second part of expiration, as is apparent from examination of the paintbrush flow-volume loops (Figs. 3-16B and 3-17B). In addition, a considerable delay in onset of inspiratory Eint activity was consistently observed when expiratory Eint activity was present, and inspiratory activity usually persisted into expiration. Thus, in this second type of Eint activation pattern, inspiratory Eint was associated primarily with the second part of inspiration and expiratory Eint was associated with the second part of expiration. In certain foals, both patterns of Eint activation were observed in the same study (Fig. 3-18).

Phasic abdominal muscle activity during expiration was consistently recorded from every standing foal from day 2 to 1 year of age. At all ages, the average onset of Eabd lagged the onset of expiratory flow (Table 3-9). However, with increasing age the magnitude of the delay increased considerably, from 0.036 ± 0.034 seconds at day 2 of age to 1.43 ± 0.42 seconds at one year of age. However, as T_E increased during the same time period, the increase in lag time could have been solely a result of the prolongation of T_E. Therefore, in order to detect any change associated with maturation in the timing of Eabd activity within expiration, the lag time was also expressed as a percent of T_E. From day 2 to 6 months of age, the onset of Eabd as a percent of T_E also increased progressively from 5.5% at day 2 to 50.8% at 6 months of age. After this time, no further changes were noted. Thus, with growth, the onset of abdominal muscle activity occurred progressively later in expiration. This finding is consistent with the increasingly biphasic expiratory flow pattern observed during the same time period. When Eabd was detected from early expiration, airflow was frequently monophasic, with a box-like configuration (Fig. 3-19A), while when onset of Eabd occurred later in expiration, a more biphasic pattern could be appreciated (Fig. 3-19B). In several of the yearling foals, following passive deflation, airflow nearly reached zero before the abdominal muscles were activated, and a mid-expiratory pause resulted (Fig. 3-20). In most foals, Eabd activity ended prior to or at end-expiration (Figs.

3-15, 3-17, 3-18), but in a few (Fig. 3-19A and B), persistence of the activity into inspiration was noted.

Representative digitized tracings of Pes, Pga, Pdi, Vt, and $\dot{V}$ at most time periods studied are displayed in Fig. 3-21, panels A-L, and the average changes in Pga (ΔPga_{maxI} and ΔPga_{maxE}) and Pes (ΔPesmax) during the breathing cycle are listed in Table 3-10. The changes in Pes associated with inspiration remained fairly constant through the first year of life, and the values (Table 3-4) were not significantly different from those measured in the adult horse (Chapter I, Table 1-3). Two peaks of Pga, one associated with the last part of inspiration and one with the last part of expiration, were observed in all standing foals. This pattern was consistently observed even in the youngest foals (Fig. 3-21, panels A and B), regardless of whether the airflow pattern was monophasic or biphasic in nature. After a maximum value was reached in late expiration, Pga decreased to a variable degree during the first part of inspiration in spite of the fact that in most of the foals less than one year of age, inspiratory muscles were activated prior to the onset of inspiratory flow. There were no statistically significant changes seen with increasing age in the magnitude ofΔPgamax during either inspiration or expiration (Table 3-10). The Pdi reached a minimum value (representing the maximal generated pressure) near the end of inspiration in all foals studied. In approximately 75% of the studies, Pdi decreased to a

Table 3-10. Pressure changes during quiet breathing in the normal foal during the first year of life.

Age	ΔP_{esmax} (cmH_2O)	C_{dyn} (L/cmH_2O)	C_{dyn}/kg ($mL/cmH_2O/kg$)	R_{pul} ($cmH_2O/L/min$)	R_{pul}/kg ($cmH_2O/L/min/kgx1000$)	R·C (s)	ΔP_{gamaxI} (cmH_2O)	ΔP_{gamaxE} (cmH_2O)
Day 2	6.98 ±4.20	0.113^{hij} ±0.041	2.84 ±0.94	0.046 ±0.016	1.19 ±0.46	0.31 ±0.16	1.15 ±0.58	3.32 ±2.31
Week 1	6.65 ±3.04	0.149^{hij} ±0.049	3.28 ±1.10	0.050 ±0.028	1.09 ±0.56	0.41 ±0.18	1.90 ±1.11	3.31 ±0.75
Week 2	8.54 ±1.4	0.099^{hij} ±0.015	1.66 ±0.36	0.116 ±0.091	1.83 ±1.25	0.66 ±0.45	1.76 ±0.71	4.36 ±2.72
Week 4	5.62 ±2.03	0.192^{ij} ±0.078	2.59 ±1.14	0.057 ±0.026	0.76^{c} ±.32	0.61 ±0.25	2.42 ±0.68	4.88 ±2.61
Month 2	5.80 ±1.74	0.204^{ij} ±0.112	1.93 ±0.95	0.079 ±.031	0.75^{c} ±.24	1.07 ±1.00	2.01 ±1.1	3.69 ±2.45
Month 3	6.45 ±1.72	0.245^{ij} ±0.64	1.78 ±0.35	0.057 ±0.028	0.42^{c} ±.19	0.87 ±0.57	3.19 ±1.75	4.69 ±1.12
Month 6	7.92 ±2.56	0.366^{j} ±.090	1.75 ±0.56	0.086 ±0.065	0.39^{c} ±0.25	1.94 ±1.69	2.08 ±1.63	3.70 ±1.52

Table 3-10. continued

Age	ΔP_{esmax} (cmH_2O)	C_{dyn} (L/cmH_2O)	C_{dyn}/kg ($mL/cmH_2O/kg$)	R_{pul} ($cmH_2O/L/min$)	R_{pul}/kg ($cmH_2O/L/min/kg \times 1000$)	R·C (s)	ΔP_{gamaxI} (cmH_2O)	ΔP_{gamaxE} (cmH_2O)
Month 9	7.67 ±1.63	0.482^{j} ±0.078	1.84 ±0.37	0.064 ±0.047	0.25^{ac} ±0.19	1.91 ±1.47	2.00 ±1.85	5.23 ±4.67
1 Year	6.42 ±1.76	0.696 ±0.168	2.30 ±0.617	0.026^{c} ±0.009	0.09^{abc} ±.03	1.05 ±0.35	3.12 ±1.88	7.82 ±1.98
means ± SD	NS		NS			NS	NS	NS

NS = not significant.

ΔP_{esmax} = maximal change in P_{es} from end expiration to most negative value during inspiration. ΔP_{gaImax} + ΔP_{gaEmax} = maximum change in gastric pressure during inspiration and expiration, respectively. C_{dyn} = dynamic compliance, R_{pul} = total pulmonary resistance, R·C = estimate of expiratory time constant, product of resistance, and compliance. a = value is significantly less than that at day 2; b = value is significantly less than that recorded on day 7; c = value is significantly less than that on day 14; h = value is significantly less than that at 6 mo. of age; i = value is significantly less than that recorded on month 9; j = value is significantly less than that recorded at 1 year of age.

Values for n are: day 2 = 6; week 1 = 6; week 2 = 6; week 4 = 8; month 2 = 5; month 3 = 4; month 6 = 4; month 9 = 5; year 1 = 5.

variable extent through the second part of expiration. Although this tendency could be appreciated in several of the foals less than one week of age (Fig 3-21, panels A and B), the decline was more pronounced and most consistently seen in the yearling foals (panel L). With a few exceptions (panel F), in the majority of foals 6-7 months of age or less, the time at which Pdi began its inspiratory descent (Fig. 3-21, panel J, point A) coincided with, or shortly lagged (by a mean of 0.02 ± 0.03 sec. at day 2 of age, and 0.03 ± 0.03 sec. at 6 months) the onset of inspiratory flow. However, at one year of age, all 5 foals consistently showed a different Pdi pattern in which the descent of Pdi lagged the onset of inspiratory flow by an average of 0.61 ± 0.36 sec., which was significantly different than the value at all other ages except that at 9 months of age (0.16 ± 0.23 sec.). An example of the typical yearling Pdi pattern are illustrated in Fig. 3-21, panel L. The beginning of the downward deflection of Pdi to its minimum value was more closely associated with the low point in inspiratory flow than with the onset of inspiratory flow (Fig. 3-21, panel L, point B). In these foals, Pdi decreased markedly during the last part of expiration, but increased from the onset of inspiratory flow through the first phase of inspiration.

The airflow patterns, EMG activities and generated pressures outlined above were measured from a relatively small number of breaths during segments of regular, quiet breathing in the standing foal. In order to acquire an idea of how representative these values were of the overall breathing pattern of the foals at the different ages studied, continuous tracings of the parameters recorded over longer periods of time, were examined. At all ages studied, when the foals were standing quietly, regular, even breathing was by far the dominant breathing pattern observed (Fig. 3-21), and in many studies, there was surprisingly little breath-to-breath variation in the configuration of the flow-volume loops. In general, the largest source of variability both between and within foals, particularly in the older foals, appeared to lie in the degree of biphasic flow associated with both inspiration and expiration. In 3 of the older foals, triple peaks of inspiratory flow were observed quite often, while expiratory flow remained biphasic (Fig. 3-22). In all ages of foals, the most frequently observed departures from the regular pattern of breathing were sighs, short periods of apnea, which almost always followed a sigh, and short interruptions of expiratory flow often associated with swallowing. All of these events occurred sporadically and infrequently in the standing position. The configuration of a typical sigh and the EMG activity and gastric pressure deflection associated with it are shown in Fig. 3-23. After initial evaluation of only the flow-volume loop, the apnea following the sigh was thought to be central in origin. However, when the flow pattern was evaluated together with the Eabd and Pga tracings it was clear that the abdominal muscles were active during the pause and were probably pushing against an obstructed upper airway. Although short central apneas were occasionally observed in the standing foal, the most common type was obstructive in nature. The pattern of expiratory flow interruptions will be presented below in the section on breathing pattern in the laterally recumbent foal.

Dynamics of Breathing in the Standing Foal During Growth.

Mean values for Cdyn, Cdyn/kg, Rpul, Rpul/kg, and the product of Cdyn and Rpul, RC, are presented for each age studied in Table 3-10. The regression equations relating the same variables to age are listed in Table 3-2, and plots of these equations for Cdyn/kg and Rpul/kg are illustrated in Fig. 3-24. Allometric equations for the two variables are listed in Table 3-3, and plots of these equations are shown in Fig. 3-25. The Cdyn increased linearly with age and body weight ($P < 0.001$), and the slope of the allometric equation was slightly less than unity (0.93). When normalized to body weight, there were no statistically significant changes in Cdyn/kg during the first year of age, and values for 7-day-old and yearling foals were not significantly different than those of the adult horses (Table 3-4). However, there was a tendency for Cdyn/kg to be lower in the middle age groups (month 2 to month 6), compared to both the younger and older foals (Fig. 3-24, panel A). While there were no clear cut trends associated with maturation in Rpul during the first year of life (Table 3-10), Rpul at one week and one year of age were both significantly greater than that of the adults. Total pulmonary resistance on a body weight basis decreased markedly in a curvilinear fashion with increasing age (Fig. 3-24, panel B). There was a considerable amount of variability in measurements of Rpul between and within foals, and the values computed for RC reflect this variation (Table 3-10). Overall, there was a tendency for RC to increase with age, although the differences were not statistically significant.

Breathing Pattern of the Laterally Recumbent Foal

Most foals one month of age and less were studied in both standing and lateral positions. Ventilatory, pressure and timing parameters for the two positions are listed and compared for each of the 5 age groups in Table 3-11. Although the differences between values recorded in lateral and standing positions were not always statistically significant, similar trends were noted at all ages. In all 5 age groups, Vt was lower in the lateral position, significantly so at days 7, 14 and 30, while f tended to increase slightly. As a result of these differences, lateral values for both $\dot{V}_E$ and $\dot{V}_{meanI}$ were somewhat lower as well. Another consistent finding associated with a change to the lateral position was an increase in the T_I/T_E ratio, which was due primarily to a shortening of T_E. A decrease in T_E was seen at all ages studied, while the direction of changes observed in T_I was variable. At all ages, there was a tendency for ΔPgamax during expiration to be smaller in

Table 3-11. Respiratory parameters measured in lateral recumbency (active abdomen, awake) vs standing for foals day 2 to 1 month of age.

	Day 2		Week 1		Week 2		Week 3		Month 1	
Parameter	Lat	Stand	Lat	Stand	Lat	Stand	Lat	Stand	Lat	Stand
V_T (L)	0.57 $\pm$0.07	0.65 $\pm$0.15	0.69* $\pm$0.20	0.80 $\pm$0.17	0.70* $\pm$0.09	0.82 $\pm$0.08	0.74 $\pm$0.09	0.80 $\pm$0.10	0.90* $\pm$0.09	0.98 $\pm$0.12
f (BPM)	56.2 $\pm$9.3	53.9 $\pm$9.9	43.8 $\pm$6.6	40.9 $\pm$5.16	40.0 $\pm$7.5	37.6 $\pm$10.7	37.8 $\pm$9.8	37.7 $\pm$9.6	36.0 $\pm$7.7	34.1 $\pm$10.6
$\dot{V}_E$ (L/min)	31.2 $\pm$3.9	34.8 $\pm$12.0	30.0 $\pm$10.8	33.9 $\pm$7.5	27.9 $\pm$5.5	30.1 $\pm$6.5	27.8 $\pm$8.5	30.7 $\pm$11.2	31.6 $\pm$4.4	32.4 $\pm$8.5
$\dot{V}_{meanI}$ (L/min)	61.5 $\pm$10.2	73.9 $\pm$33.0	49.1* $\pm$9.3	60.6 $\pm$5.7	52.0 $\pm$11.9	57.2 $\pm$13.9	52.6 $\pm$14.1	60.1 $\pm$24.1	55.8 $\pm$8.5	63.6 $\pm$17.9
T_I/T_E	0.89 $\pm$0.24	0.79 $\pm$0.15	1.07* $\pm$0.11	0.96 $\pm$0.16	1.03 $\pm$0.15	0.97 $\pm$0.18	1.07 $\pm$0.12	0.97 $\pm$0.17	1.16* $\pm$0.21	0.93 $\pm$0.20
T_I (sec)	0.51 $\pm$0.09	0.51 $\pm$0.15	0.74 $\pm$0.13	0.72 $\pm$0.09	0.79 $\pm$0.17	0.84 $\pm$0.27	0.87 $\pm$0.20	0.82 $\pm$0.20	0.93 $\pm$0.16	0.94 $\pm$0.34
T_E (sec)	0.60 $\pm$0.16	0.65 $\pm$0.10	0.70 $\pm$.12	0.75 $\pm$0.17	0.83 $\pm$.20	0.90 $\pm$0.34	0.82 $\pm$0.23	0.87 $\pm$0.25	0.84 $\pm$0.23	1.06 $\pm$0.53

Table 3-11. continued

	Day 2		Week 1		Week 2		Week 3		Month 1	
Parameter	Lat	Stand	Lat	Stand	Lat	Stand	Lat	Stand	Lat	Stand
ΔP_{gaE}	1.43* ±0.50	3.32 ±2.3	1.55* ±0.81	3.26 ±0.65	3.28 ±1.72	4.88 ±2.68	2.53 ±1.33	3.77 ±2.23	3.30* ±1.54	4.88 ±2.61

means ± SD

*Significantly different from standing ($p < 0.05$).

V_T = tidal volume, f = frequency, $\dot{V}_E$ = instantaneous minute ventilation, $\dot{V}_{meanI}$ = mean inspiratory flow, T_I = inspiratory time, T_E = expiratory time, ΔP_{gaE} = change in gastric pressure during expiration.

lateral recumbency than in the standing position. Dynamic compliance values in the lateral position were influenced by the consistent presence of an artifactually positive Pes tracing during expiration. This artifact most likely resulted from the weight of the mediastinal structures exerting pressure on the esophagus, and was therefore unavoidable. Therefore, Cdyn values obtained in this position were not used for any comparisons.

The breathing pattern that the foals utilized to achieve minute ventilation while in the lateral position differed in some ways from that observed while standing. Five of the 10 foals each displayed two distinct patterns of expiration at one or more of the ages studied: the first appeared to be a complete passive deflation and the second was at least in part active with evidence of abdominal contraction, similar to that consistently seen in the standing position. For the remaining 5 foals, all expirations analyzed involved the use of the abdominal muscles. Examples of the active and passive patterns are illustrated in Fig. 3-26, panels A-B and C-D, respectively. In the active expiration (panel A), a peak of Pga during expiration was observed concurrently with Eabd activity, which resulted in generation of box-like, very slightly biphasic flow-volume loop (panel B). When Eabd was undetectable and Pga was flat during expiration (panel C), the linearity of the expiratory limb of the flow-volume loops was consistent with a passive, uninterrupted deflation to or near to Vrx at end-expiration (panel D). The frequency of occurrence of the passive pattern appeared to decrease with increasing age. For example, at day 2 of age, both active and passive patterns were detected in 5 of the 7 foals studied, and the other 2 solely utilized the active pattern during the period studied. On the other hand, at day 30, of the 8 foals studied, only 2 were found to utilize both patterns, while the other 6 appeared only to actively expire. When major parameters of ventilation and timing in the passive pattern were compared to those of the active pattern, with the exception of the maximum change observed in Pga during expiration, no significant differences were found between the 2 patterns. The transition from active to passive expiration appeared to be most frequently associated with sleep. The passive pattern was observed only during sleep in 3 of 5 foals, was seen during both sleep and wakefulness in one foal, and only in the awake state in the other.

In general, the transition from wakefulness to sleep was characterized by marked irregularities in both frequency and pattern of breathing (Fig. 3-27). The irregularities in breathing pattern were usually accompanied by muscle twitches, rapid-eye-movements, and limb movements typically associated with active or rapid-eye-movement (REM) sleep. Interruptions of expiratory flow, presumably resulting from laryngeal adductor activity, were much more frequently observed during sleep than in the awake state. Examples of typical airflow patterns of breaths with expiratory obstructions are illustrated in Fig. 3-28 along with EMG and pressure data. In the majority of obstructed expirations in certain foals, concurrent with the release of the obstruction, the abdominal muscles were activated late in expiration (Fig. 3-28, panel A), In others foals, the Pga and Eabd tracings indicated that the abdominal muscles were not activated at that time (Fig. 3-28, panel B). Although expiratory obstructions were observed more frequently in the sleeping foal, they were also occasionally observed during awake breathing in lateral recumbency. The frequency of observation of this pattern did, however, seem to decrease with increasing age.

As was found in the adult horses in Chapter I, in the foal studies, the RIP-generated flow-volume loops acquired with the facemask in place were not appreciably different than those obtained when the facemask was absent (Fig. 3-29).

Discussion

Changes in Ventilatory Parameters Associated with Growth

In the growing foal, minute ventilation increased during the first year of life, due to a progressive rise in tidal volume in spite of a pronounced decrease in respiratory frequency. However, when normalized for body weight, the mean value for $\dot{V}_E$/kg was high (848 ml/min/kg) in the 2-day-old foal relative to that (162 ml/min/kg) of the adult horse (Chapter I). The time course of this decline with maturation followed a curvilinear function with the slope of the line steepest during the first 3 weeks of age. The decline in $\dot{V}_E$ was due to a substantial decrease in the frequency of breathing, while Vt/kg remained fairly proportional to the foal's size. The substantial decrease in frequency observed during the first year of life was a result of a prolongation of both T_I and T_E. There was a disproportionately larger increase in T_E compared to T_I, which resulted in a significantly lower T_I/T_E ratio in the older foals. Normalized values for mean inspiratory and expiratory flows decreased with age in a pattern very similar to that of $\dot{V}_E$/kg. Thus, in order to meet its relatively high ventilatory requirements, the young foal appeared to adopt a breathing strategy with a high frequency of breathing, rather than a large Vt, a pattern which necessitates high flow rates to move sufficient air in and out of the lungs in the time allotted for the breathing cycle.

It is probable that $\dot{V}_E$/kg was initially elevated as a result of a high metabolic rate in the newborn foal. Although the mechanisms involved are not completely understood, a high oxygen consumption ($\dot{V}_{O2}$) has been reported in many species of newborns (Hill, 1959), including the foal (Stewart et al., 1984). A number of factors, ranging from an increased level of sympathetic activity to increased work of breathing in the neonate have been proposed as possible explanations. Bartlett and Areson (1977) used allometric equations to compare both alveolar surface area and oxygen uptake to body weight in a wide range of newborn animals, from the mouse to the calf (but not the foal). A constant allometric relationship between oxygen consumption and body weight had previously been observed among adults of many species (Brody, 1945), with an exponent equal to approximately 0.7. As this value is less than unity, $\dot{V}_{O2}$ increases at a rate slower than body weight, and therefore, $\dot{V}_{O2}$ on a per kg basis would be expected to be smaller in the larger species. Bartlett and Areson (1977) found a substantial deviation from this pattern in both small and large neonates. Newborn mice and rats had lower metabolic requirements than predicted from the adult relationship, while the newborn calf more rapidly consumed oxygen than adult species of the same body weight. The authors explained this finding by the fact that newborns of larger species are more mature and therefore more active at birth than are smaller animals. In addition, they found that the relationship between oxygen consumption and surface area of the lungs ($SA/\dot{V}_{O2}$) in the same neonatal species also differed from that previously described for adults (Tenney and Remmers, 1963). The calf and the lamb had $SA/\dot{V}_{O2}$ ratios higher than those of comparably sized adults, while the smaller neonates had lower ratios than those of the adults. It was proposed that this pattern was consistent with the extensive metabolic requirements which accompany the large neonates' level of activity and the need for effective thermoregulation in an often unprotected environment. On the other hand, the species with a lower SA/$\dot{V}_{O2}$ ratio are usually well-protected in nests or burrows, with a very low level of activity, and probably only rarely need to raise their metabolic rate above resting levels. This line of reasoning could be applied to explain the initially high $\dot{V}_E$/kg in the foal as well, as the level of activity and need for thermoregulation in this species is of the same or greater magnitude as that of the lamb and calf, it not greater, and is probably greater during the postnatal period than at any other time in its development.

Several previous studies (Gillespie, 1975; Rossdale, 1969; Stewart et al., 1984) also reported high $\dot{V}_E$/kg values relative to the adult horse in normal newborn foals. The characteristics of the transition to adult values, however, have not been reported for this species; the longest period that these values have previously been followed postnatally was 14 days. Although certain ventilatory parameters were studied at different ages in Dutch Friesian cattle (Lekeux et al., 1984), the age groupings (group 1, mean = 17 days; group 2, mean = 135 days) and time period studied (to almost 2 years of age) limited the number of meaningful comparisons that could be made to the present study. However, from comparison of slopes of the regression equations, minute ventilation in the cattle appeared to increase at a greater rate than the foals with growth. This appeared mainly due to a consistently higher respiratory rate in the older calves than in the older foals (23-26 vs. 12-15 BPM, respectively), while respiratory rates were similar in the younger animals. As in the foals, Vt/kg in the calves remained relatively constant during the period studied, averaging approximately 9 ml/kg. There was only a slight tendency for a decrease in the T_I/T_E ratio with age.

The majority of reports on the effect of growth on ventilatory parameters have involved species that are considerably less mature than the foal at birth. And as one might expect from the previous discussion, the pattern of maturation of ventilatory parameters observed in the foal did differ in certain ways from those reported in smaller species. In a study of changes in ventilation of the neonatal rabbit during the first week of age, Wyszogrodski et al. (1978) reported that although f decreased with age, the value of $\dot{V}_E$ normalized to body weight ($\dot{V}_E$/BW) remained nearly constant because of an significant increase in Vt/BW. The frequency of breathing decreased as a result of an equal prolongation of T_I and T_E, and therefore T_I/T_E also remained constant. Mean inspiratory flow/BW also remained constant in the rabbit during the period studied. In a study of postnatal maturation of ventilation in the kitten during the first 8 weeks of life, Marlot et al. (1984) found that $\dot{V}_E$ increased as a result of a rise in Vt and fall in f. Although reported values were not normalized to body weight, calculations from their data plots suggest that $\dot{V}_E$/BW was roughly half the value at 8 weeks of age compared to newborn values, while, in contrast to the rabbit, Vt/BW remained constant with maturation. The ratio of T_I to T_E also remained constant with increasing age in the kitten as well as in the human infant when studied over the first 4 months of age (Haddad et al., 1979). In humans, the relationship of Vt to body weight has also been found to remain relatively unchanged through life while the alveolar ventilation/BW ratio ($\dot{V}_A$/kg) in the adult is roughly half the newborn value (Polgar and Weng, 1979). As the ratio of physiologic and anatomic dead space to tidal volume or body weight has not been found to change with development (Nelson, 1966), $\dot{V}_E$/kg would be expected to follow the same trend as $\dot{V}_A$/kg.

Certain differences between maturational studies in the smaller mammalian species, such as the rabbit, and the foal could result from differences in maturity of these species and their respective respiratory systems at birth, as previously discussed. The rabbit is an immature neonate and its respiratory parameters might be expected to change more extensively during development to adulthood. However, the rabbit study was only continued through the first postnatal week, and different conclusions may have been drawn if the rabbits had been studied over a longer period during development.

The mechanism underlying the differences between the foal and other species in maturational changes of timing parameters must remain speculative. The foal appears to be the only species studied to date in which f decreased as a result of a disproportionate prolongation of T_I and T_E. An explanation may relate to the observation that the horse is also the only species in which a transition with age from a monophasic to a polyphasic breathing pattern has been described. Even in monophasic breathers, the control mechanisms responsible for the lengthening of T_I and T_E during growth are poorly understood. There is some evidence to suggest that the prolongation of T_I is related, at least in part, to an increase in the activity of the bulbospinal inspiratory neurons, as Marlot and Duron (1981) showed that the percentage of early active inspiratory phrenic motoneurons increased with increasing postnatal age in the kitten. A decline in inspiratory-inhibitory feedback from the vagally mediated inflation reflex (Gaultier and Mortola, 1981) and a reduction of the intercostal-to-phrenic inhibitory reflex as chest wall distortion decreases with maturation (Trippenbach et al., 1982) have also been suggested as possible mechanisms responsible for the increase in T_I in growing kittens (Marlot et al., 1984). Duration of T_E in many neonatal mammals is partially dependent on vagal activity. In the newborn kitten, it has been shown that the percentage of tonic pulmonary stretch receptors is lower than in adult cats (Marlot and Duron, 1979; Marlot et al., 1982; Schweiler, 1968). This finding could partially explain the shorter T_E in the newborn (Marlot et al., 1984). Which, if any, of these mechanisms influence timing parameters in the growing horse is unknown, but it seems reasonable to expect that a transition to a polyphasic airflow pattern might involve changes in central and/or peripheral control of inspiration and/or expiration.

In the present study, values of $\dot{V}_E$ and $\dot{V}_E$/kg reported for normal foals during the first week of age were higher than those previously reported for normal unanesthetized foals. While my value for Vt/kg in the 24 hour old foals was very similar to that (15.3 ml/kg) reported by Gillespie (1975) in a small group of young foals, values for f were somewhat lower, which resulted in a lower $\dot{V}_E$/BW (mean = 498 ml/min/kg). In normal Thoroughbred foals between 24 and 48 hours of age, Rossdale (1969) reported Vt to be 0.56 ± 0.02 L (mean ± SE), f to be 35.4 ± 1.5 BPM, and $\dot{V}_E$ to be 19.3 ± 0.8 L/min. In the present study, values for the frequency of breathing were comparable to those found by Stewart et al. (1984) in a group of Thoroughbred foals studied on 1, 2, 3, 4, 7, and 14 days of age. However, her values for Vt (and therefore $\dot{V}_E$) at each age studied were less than one-half the values found in the present studies. There are several possible explanations for these discrepencies. First, the amount of dead space of my facemask system could have been sufficient to stimulate an increase in $\dot{V}_E$. However, the dead space of the equipment used in the present study was comparable to that reported in Gillespie's study. He calculated that an addition of 50 ml would increase the dead space of the foal by only about 10% and concluded that this amount would not have induced rebreathing sufficient to have substantially influenced his measurements. Careful observation of the breathing frequency and pattern of my foals, with and without the facemask in place, did not disclose any observable differences. Thus, it is doubtful that rebreathing was a significant factor during the present studies. However, it is feasible that some excitement and struggling associated with the restraint and instrumentation of the foals could have caused an increase in f and/or Vt and thus produced artificially high values for resting conditions in the young foals. However, the youngest foals tolerated the handling procedure remarkably well. After being placed in lateral recumbency and instrumented, they usually relaxed and frequently went to sleep. The frequency of breathing recorded in the relaxed foal in lateral recumbency was actually slightly but consistently higher than in the standing foal. Segments of breathing recorded during or just following a period of activity or struggling were not included in the analysis. In addition, the respiratory rate and breathing pattern of most of the foals at rest with their mothers prior to the studies closely matched the resting rate and pattern observed during the study. From evaluation of the individual foal values, it was clear that the high average value for $\dot{V}_E$/kg did not result from one or two abnormal individuals. Rather, the average respiratory rate of every foal studied at day 2 of age (which ranged from 41 to 64 breaths per minute) was higher than the previously reported values. For these reasons, it is unlikely that the restraint and measurement techniques utilized substantially influenced the resting ventilatory parameters obtained.

If the values obtained for $\dot{V}_E$/kg in the group of foals were not falsely elevated due to methodological error, what physiological explanation is there for this finding? Although the thermoneutral zone has not been established for the foal, it is doubtful that any of the foals were placed under cold stress that would have caused an elevation in metabolic rate. All of the foals were born between July and October in central Florida, and the weather was usually hot (daytime high = 85-100°F) and humid at this time of year. It did seem, however, that the foals with the highest recorded respiratory rates were studied on the hottest, most humid days. Although the temperature of the study room was fairly well controlled, it is possible that the increased respiratory rates were the result of efforts by the foal to dissipate heat. Unfortunately, virtually nothing is known about the thermoregulatory strategy utilized by the neonatal foal.

With the possible exception of the influence of climate, it is unlikely that this population of foals was appreciably different from those studied in previous reports. The mares and foals were housed and fed in a conventional manner, the foals were of appropriate size for their breed, and every attempt was made to rule out clinically or radiographically apparent respiratory disease prior to each breathing study. It was concluded that the measurements obtained were representative of normal resting values in the unrestrained foal. However, the ventilatory parameters reported in this study should not necessarily be considered as normal values for all breeds of foals under all circumstances in all types of environments.

In comparison of allometric equations relating the major ventilatory parameters and subdivisions of lung volume to body weight, it was found that that the slopes or exponents of the equations for total lung capacity (Fig. 2-8) and Vt (Fig. 3-7) were virtually identical (0.863 vs 0.865). In addition, the same trend toward lower TLC/kg values in the 3-6 months old foals (Table 2-3) was also observed in the Vt/kg values. The ratio of Vt/kg reached a minimum at 2 months of age and like TLC/kg, also increased slowly from that time to 1 year of age. The consistency of the developmental relationship between body weight and these two lung volumes, measured by considerably different methods under very different circumstances suggests that lung growth in the horse may be dysanaptic, with increases in overall body size well exceeding lung growth in the maturing foal during the first year of life.

Breathing Pattern in the Foal During Growth

Breathing pattern in the standing foal. The results of the awake breathing studies in the standing position both confirmed the observation made in preliminary studies that the pattern of airflow in neonatal foals is essentially monophasic and supported the hypothesis that a transition is made to a biphasic flow pattern within the first year of life. During awake breathing in the standing position in all age groups of foals studied, the most commonly observed breathing pattern was regular in depth and frequency. The configuration of the flow-volume loops in the newborn foals did vary from essentially box-like to a pattern with slight inflections suggesting the beginning of a biphasic flow pattern (Fig. 3-11, panel A and B), particularly during expiration. However, no awake foal less than one month of age showed an adult-like polyphasic pattern of breathing. The transition to the adult strategy appeared to occur in stages. By 3 months of age, in most foals, an often prominent biphasic expiration was consistently noted, and in the subsequent studies, the peak expiratory flows became progressively larger, while the mean values for $\dot{V}_{Edip}$ remained approximately the same (Table 3-8), accentuating the biphasic character of expiration in the older foals. In several individual foals, expiratory flow actually neared zero at mid-expiration. In addition, $\dot{V}_{Epeak1}$ and $\dot{V}_{dip}$ both occurred progressively earlier in expiration with increasing age. The pattern of change of inspiratory flow with age was not as consistent, but there was rarely a substantial inflection observed in the inspiratory flow tracing until the 6 month studies. During the subsequent studies, it was not until the 1 year studies that an obvious polyphasic inspiration was consistently seen in all foals, although some yearling foals showed more of a biphasic inspiration than others. The strong resemblance of the timing and flow pattern of adult and yearling composite breaths suggests that by 1 year of age, the average foal had acquired an adult pattern of breathing.

Analysis of the overall pattern of respiratory muscle activation with respect to airflow revealed important differences between the neonatal and adult horse. In all foals less than 1 month of age, onset of Edi consistently preceded the onset of inspiratory flow and it was not until the 1 year studies that Edi onset lagged inspiratory flow in the majority (4 of 5) of foals. Thus, in contrast to the adult horse in which a passive component of inspiration was also observed, but similar to the pattern observed in most other species, inspiration in the neonatal foal was an active process. However, in contrast to most other species in which expiration during resting conditions has been described as a primarily passive process, expiration in the standing neonatal foal was a primarily active event. Phasic abdominal EMG activity was always observed in the standing foal. Although there was considerable individual variation, on the average, abdominal muscle EMG activity was detected early in expiration in the younger foals. The pattern of change in Eabd activity with age (Table 3-9) principally consisted of a marked increase in the delay in onset of Eabd with respect to onset of expiratory flow. Thus, with maturation, the first part of expiration, to a greater and greater extent, became a primarily passive event. As in the adult horse, the delay in activation of the abdominal muscles in the more mature foals resulted in an obvious second peak of expiratory flow (Fig. 3-20).

Two distinct patterns of Eint activation were identified. In the first, most commonly observed pattern (Fig. 3-15), only inspiratory Eint activity was detectable, and onset of Eint preceded or in the older foals, only shortly lagged the onset of inspiratory flow. In the second pattern (Fig. 3-16 and Fig. 3-17), which was usually observed in one or two foals at each age studied (but not necessarily the same individuals each time), both inspiratory and expiratory Eint activity was obvious. When activity of both inspiratory and expiratory intercostal muscles was present, there was usually a marked delay in onset of Eint relative to both inspiratory and expiratory airflow. As shown in Fig. 3-18, both patterns were occasionally observed during the same study. Neither the control mechanisms responsible for generation of these patterns or the reasons that one pattern might be utilized over the other are well understood. However, from limited observation of transitions between the two patterns, subtle changes in posture and weight distribution may influence which pattern is detected. As was noted in the adult horses, it is probable that the intercostal muscles are responsible for a number of activities primarily non-respiratory in nature, such as stabilization of the rib cage and maintenance of posture during both rest and exercise.

There appeared to be a strong temporal relationship during growth between the timing of changes observed in airflow pattern and EMG activation pattern. Early activation of inspiratory and expiratory respiratory muscles in the younger foals was associated with a flow pattern essentially monophasic in character. The increasing biphasic character of expiration appeared concurrently with the increase in delay of onset of Eabd, while a biphasic inspiration was not consistently observed until a consistent lag in onset of Edi was also noted, at 1 year of age. Tracings from individual horses tended to support these conclusions. For example, one 1-month-old foal (Fig. 3-14) displayed a much more prominent biphasic inspiratory and expiratory flow pattern than the other foals studied at that age. She also was the only foal of that age in which a delay in onset of Edi was found.

The patterns of change observed in Pga and Pdi during the breathing cycle were consistent with the EMG and airflow data. The configuration of the Pga tracings against time in all ages of foals studied (even the youngest ones) was very consistent and very similar to that described in the adults in Chapter I. One peak of Pga was associated with the latter part of inspiration and a second, higher peak of Pga was observed during the last part of expiration, regardless of whether expiratory flow was monophasic or biphasic. As in adults, the expiratory peak of Pga in all foals was consistent with activation of the abdominal muscles and the inspiratory peak with activation and caudal displacement of the diaphragm. The abdominal muscles appeared to be more effective abdominal pressure generators than the diaphragm, as Pga consistently rose to a greater extent during expiration. This could be due to the anatomical arrangement of the abdominal muscles and an associated mechanical advantage. Although there was a slight tendency for ΔPga_{maxE} to increase with age, the magnitude of the change was insufficient to by itself account for the marked increase in biphasic flow pattern observed during maturation.

Peak generated Pdi (the most negative value) also occurred during the Pdi was observed during the last part of inspiration reflecting maximal diaphragmatic effort, analagous to inspiration in other mammals. In the majority of the younger foals, the onset of decline of Pdi (Fig. 3-21, panel J, pt. A) to its mimimum value during inspiration was closely associated with the onset of inspiratory flow. This was consistent with the finding that the time of onset of Edi activity usually preceded the onset of inspiratory flow. A clearly different type of inspiratory Pdi tracing was occasionally observed in the 6 and 9 month old foals, and consistently observed in all 5 foals studied at 1 year of age. In this pattern, the beginning of the decline in Pdi was much more closely associated with $\dot{V}_{Idip}$

rather than the onset of inspiratory flow (Fig. 3-21, panel L, pt. B). In addition, from a minimum expiratory value at end-expiration, Pdi actually increased (toward zero) during the first part of inspiration. This pattern is consistent with the first part of inspiration being a primarily passive event, with a delay in a transdiaphragmatic pressure generation during inspiration until actual diaphragmatic contraction occurs.

In summary, the changes in pattern of airflow, sequence of respiratory muscle activation and generated pressures observed allow a consistent description of the maturation of breathing pattern of the horse during the first year of life. By one year of age, foals displayed essentially the same breathing pattern described in adult horses in Chapter I, utilizing a combination of active and passive inspiration and expiration to breathe around, rather than from, Vrx. On the other hand, in the neonatal foals, inspiration and expiration were both primarily active, and airflow pattern was essentially monophasic in nature. Maturation to the adult breathing pattern appeared to involve a delay in activation of both inspiratory and expiratory muscle groups, establishing a passive and active component to both inspiration and expiration. Throughout the study period, concurrent with the increase in delay of abdominal muscle EMG activation, the expiratory flow pattern became progressively more biphasic in appearance. The time of appearance of a consistent biphasic inspiratory flow pattern was considerably later, at approximately one year of age, and coincided with the appearance of a delay in inspiratory muscle activation.

Relationship of EEV to Vrx in the growing foal. In the yearling foals, the delay of inspiratory muscle activation relative to the onset of inspiratory flow, the biphasic inspiratory flow pattern, and a mid-expiratory pause in flow were strong indications that EEV was substantially below Vrx, as described in adult horses in Chapter I. In the younger foals, however, which typically utilized an essentially monophasic airflow pattern, it could not be conclusively established whether the foals were breathing from, above, or below Vrx. The major difficulty in determination of the position of EEV relative to Vrx lay in the fact that these individuals persistently used their abdominal muscles phasically during expiration and did not delay onset of inspiratory muscle activity or display a biphasic inspiration. If the expiratory muscles had been relaxed during expiration, analysis of the passive flow-volume curve could have established whether the foals breathed from or above Vrx (Griffiths et al., 1983; Kosch and Stark, 1984; Mortola et al., 1985). However, in the present studies, the slope of the deflation limb could not be assumed to represent the passive time constant of the respiratory system nor could extrapolation of the linear portion of the deflation limb to the Y-axis yield any useful information concerning the position of Vrx relative to EEV.

During analysis of the data, it became apparent, contrary to others' suggestions (Mortola et al., 1985), that expiration could not be assumed to be passive based only on the observation that the expiratory limb of the flow volume loop was linear. In Fig. 3-30, panel A, are two flow-volume loops representing the same breath; in the loop on the right, Eabd was electrically added to $\dot{V}$ to create a paintbrush flow-volume loop. Without the EMG information, the configuration of the loop would have indicated that EEV was greater than Vrx, with expiration interrupted before passive deflation to Vrx was completed. As expiration was actually active, no such conclusions could be drawn. In panel B, the linear configuration of the expiratory limb of the loop suggests the system passively deflated to very close to Vrx. However, from the superimposed EMG data and the changes in Pga in the time tracing, it was obvious that expiration was in fact active.

Some studies of breathing in human neonates have used information acquired during apneic pauses to help to explain breathing strategy and establish the position of Vrx. Olinsky et al. (1974) observed that during central apneas in premature human neonates, lung volume was considerably lower than the normal end-expiratory level during tidal breathing. He assumed that this lower lung volume represented Vrx, and that during normal breathing, EEV was actively maintained above this volume. Similar analysis of apneic pauses in the foals was not possible. Although apneas did occur that initially appeared to be centrally-mediated based on the configuration of the flow-volume tracings, concurrent Eabd and Pga recordings indicated that the abdominal muscles were usually active during the pauses (Fig. 3-23) and that some degree of airway obstruction accompanied the pauses. Thus, in the foals, prediction of the position of Vrx during apnea could not be accomplished.

Although conclusive proof cannot be provided, from the data that was acquired in this study, it appears highly unlikely that the standing neonatal foal typically breathes from above Vrx. First, neonates of other species that have an elevated EEV relative to Vrx routinely utilize mechanisms that effectively prolong the time constant by retarding expiratory airflow. Post-inspiratory inspiratory muscle activity as well as upper airway narrowing, both of which serve to brake expiratory airflow, are commonly used strategies that may delay lung deflation sufficiently to prevent complete expiration to Vrx before the next inspiration begins. In the standing neonatal foal, upper airway expiratory braking was infrequently observed, and post-inspiratory inspiratory muscle activity was in fact observed substantially less frequently in the young foals than in the older animals. Second, the consistent use of the abdominal muscles during expiration would be expected to actually aid the deflation process; the effective or active time constant in such a system would be expected to be shorter than under passive conditions. Therefore, a complete expiration to or below Vrx should actually be facilitated by such a strategy.

Analysis of the Pdi tracings provided limited evidence in support of the theory that the younger foals usually expired to a point somewhat lower than Vrx. In the standing position in the majority of foals, even in the youngest animals (Fig. 3-21, panel A and B), some decline of Pdi was observed during expiration. In the absence of artifacts associated with the pressure measurement techniques, this decrease in Pdi without concurrent diaphragmatic activation suggests that the diaphragm was being passively stretched as a result of abdominal muscle activation, as described for the adult pattern in Chapter I. Although the length-tension characteristics of the equine diaphragm are not known, in humans, this would be consistent with deflation to a lung volume less than Vrx. Very little is known about the neurological control mechanisms regulating an active expiratory process during awake breathing. It is difficult to imagine that the system would be designed so that the abdominal muscles would be shut off exactly at the right instant to allow inspiration to take place exactly from Vrx. It is more likely that end-expiratory lung volume would be somewhat less than Vrx in such a situation.

It is suggested that in the neonatal foal, EEV is not determined by an equilibrium of static forces. In contrast to reports of breathing pattern in other neonates, no evidence was found in these studies to support the idea that

EEV is actively maintained above Vrx in the term, standing foal. Rather, there is limited evidence to suggest that EEV is in fact somewhat less than Vrx, as a result of abdominal muscle activity during expiration.

Breathing pattern in the laterally recumbent foal. Some reports have suggested that respiratory function is impaired in the laterally recumbent foal. Stewart et al. (1984) reported that arterial oxygen concentration in the normal neonatal foal was lower in the lateral compared to the standing position. Substantial right-to-left shunting (16% of cardiac output) has also been reported in the laterally recumbent foal during the first days of life (Rose et al., 1983). Thus, in this study, it was hypothesized that breathing pattern would also be altered in the lateral position, in possible compensation for alterations in pulmonary function.

In the awake foal in lateral position during the first month of life, Vt, $\dot{V}_E$, and $\dot{V}_{Imean}$, and ΔPga_{maxE} were consistently lower, f and the ratio of T_I/T_E were somewhat increased compared to the standing position (Table 3-11). Although $\dot{V}_{Emean}$ remained essentially unchanged in the lateral position, the flow-volume loops generated typically displayed a slightly less prominent second phase of expiratory flow compared to those obtained in the standing position. The increase in the T_I/T_E ratio was primarily a result of a shortening of T_E. These changes are similar to those reported by Stark et al. (1984) in a report of the ventilatory effects of posture change in newborn human infants, and are compatible with vagally-mediated reflex activity. Several investigators (Bartoli et al., 1973; Grunstein et al., 1975) have suggested that absolute lung volume exerts a strong influence on expiratory timing, as an increase in lung volume was found to result in a sustained increase in T_E, while T_I appeared to be independent of changes in absolute lung volume. These changes could be abolished with vagotomy. In the foal, with a transition to the lateral position, the absolute lung volume would be expected to be decreased, due to the weight of the non-dependent lung, the heart and other mediastinal structures exerting pressure on the dependent lung, which could contribute to the decreased minute ventilation. It would also follow from the previous argument that in the lateral position, T_E should theoretically be shortened, and this was observed. Whether this pattern offers any particular advantage in terms of ventilation to the laterally recumbent foal is not known.

It was initially thought that another, more obvious explanation for these changes might be that the foals were simply more excited and active in the standing position and thus had a higher Vt and $\dot{V}_E$. However, if this were the situation, the frequency of breathing would also be expected to be elevated in the standing position and it was not. In summary, there was some evidence to suggest that associated with a change to lateral recumbency were changes in ventilatory pattern consistent with a compromise in pulmonary function. Other than a possible role of vagal timing reflexes, the mechanisms responsible for the observed changes are not known.

In lateral recumbency, the abdomen was still used phasically during expiration in almost all foals studied. However, the maximum change of Pga during expiration was consistently less than that recorded in the standing position. There are several possible explanations for this finding. First, it is possible that abdominal EMG activity was decreased during expiration in lateral recumbency. In support of this, in a study of the response of the abdominal muscles to expiratory loading in the anesthetized cat, Koehler and Bishop (1979) reported that lung volume could modulate abdominal muscle activity; at lower lung volumes, less abdominal muscle activity and abdominal pressure generation was observed. Second, a change in the orientation of the respiratory muscles to one another could occur during a position change, resulting in changes in the mechanical advantage and/or compliance of the system. In this situation, the same degree of muscle contraction might result in less actual pressure generation. Regardless of the mechanism, a decrease in effective abdominal contraction is consistent with maintenance of lung volume in lateral recumbency.

In contrast to the standing foals where abdominal muscle activity was always observed, in short segments of a few lateral studies, the abdominal muscles appeared to remain relaxed during expiration, and in these instances, complete deflation to Vrx was usually observed (Fig. 3-26). This passive expiratory pattern was most consistently associated with, but not limited to, REM sleep. A loss of active braking mechanisms during expiration in active sleep has been reported in lambs (Harding et al., 1980) and puppies (England et al., 1985). A substantial decrease of EEV has also been observed during REM sleep in human infants (Henderson-Smart and Read, 1979). Thus, in the foal it is possible that during REM sleep, the central control of another group of respiratory muscles, the abdominal muscles, is altered as well. When expiratory muscle activity was absent, the fact that the slope of the expiratory limb of the flow-volume loop was linear to its intersection with the Y-axis suggests that EEV was not appreciably different from Vrx in the laterally recumbent foal during passive expirations.

While the foals were maintained in lateral recumbency, although there were still long periods of regular breathing, the overall breathing pattern was more irregular than observed in the standing position. Much of this variability was a result of a transition to REM sleep (Fig. 3-27). In puppies (England et al., 1985), lambs (Harding et al., 1980), and human infants (Hathorn, 1975; Hoppenbrouwers, et al., 1978), the breathing pattern during REM sleep was also found to be characterized by marked variability. Although most commonly seen during sleep, sighs and inspiratory and expiratory occlusions appeared more frequently in the awake lateral position than in the awake, standing posture. An overall impression was that the frequency of both sighs and expiratory obstructions tended to decrease with increasing age, but the incidence of these variations was not quantitated. It is possible that the sighs and upper airway obstructions served to both counteract an increased tendency for atelectasis in the down lung and maintain an elevated lung volume to allow for better gas exchange. However, in several foals, concurrent with or preceding the release of the upper airway obstruction was abdominal muscle activity (Fig. 3-28, panel A). This strategy seems somewhat contraproductive in an animal attempting to defend lung volume, because, as stated previously, active expiration would be expected to cause a more rapid deflation of the lungs.

Qualitative analysis of the degree of persistence of inspiratory muscles into expiration revealed little difference between foals in lateral and standing position at a particular age group. In other words, like the situation in the standing foals, the younger the age of the foal, the less tendency there was for either persistent diaphragmatic or intercostal muscle activity into expiration. This finding differs considerably from studies conducted in normal, supine human infants (Kosch and Stark, 1984; Lopes et al., 1981) in which post-inspiratory inspiratory muscle activity was found to be an important mechanism for braking expiratory airflow and facilitating defense of lung volume. In all ages of horses, this activity may simply serve to smooth the transition from inspiration to expiration by braking potentially high flow rates, rather than defend lung volume per se.

In summary, there were obvious differences between the breathing pattern of foals in the standing and lateral position. An increase in frequency of breathing with a concurrent shortening of T_E, decreased abdominal pressure generation by the expiratory muscles, and an increased frequency of sighs and expiratory obstructions may all reflect compensatory responses due to a decrease in lung volume in lateral recumbency. However, it could not be conclusively established that the foal actively maintains EEV above Vrx while in this posture.

Finally, it should be remembered that the foals included in this study were all term, normal individuals. The breathing strategies utilized by the premature foal or by the foal with respiratory disease may be very different than those reported here. It is the author's experience that premature and otherwise compromised recumbent neonatal foals may display both markedly irregular breathing patterns and consistently audible grunts, suggestive of upper airway braking.

Changes in Dynamic Mechanics Associated With Growth

As would be expected, Cdyn increased linearly with age and body weight at a rate very similar to that reported in Chapter II, Table 2-6 and 2-8 for static lung compliance (C_L). The slopes of the allometric equations for Cdyn and C_L were both 0.93, indicating that the increase in both parameters was almost directly proportional to the increase in body weight. However, when normalized to body weight, average values for Cdyn/kg at all ages studied were to a variable degree (overall, approximately 35%) lower than values reported for C_L/kg. This systematic difference was not expected but there are several possible explanations.

First, the conditions under which each was measured varied considerably, C_L being measured in the anesthetized, paralyzed condition, and Cdyn in the awake spontaneously breathing condition. Although published data concerning the effect of anesthesia on lung compliance in other species is somewhat conflicting, the main trends reported have been either a decrease (Westbrook et al., 1973) or no change (Lai et al., 1979; Muggenburg and Mauderly, 1974) in lung compliance with anesthesia induction. Secondly, frequency dependence of compliance could explain a lower Cdyn value in the spontaneously breathing foal. However, if this mechanism was operational in the foals and there were unequal emptying rates (time constants) in different parts of the lungs, as the frequency of breathing increased, the value of Cdyn would be expected to deviate more and more from the static value. As the same magnitude of difference between Cdyn and C_L was observed regardless of the respiratory rate, this possibility was considered unlikely. Third, as compliance is lung volume dependent, and the pressure-volume relationship is linear only in the midrange volumes, a marked change in the relationships between lung volume subdivisions from awake values during anesthesia could theoretically account for a discrepency between compliance measurements. It was considered unlikely that the changes induced by anesthesia were of sufficient magnitude and consistency to satisfactorily explain the differences in compliance values. Finally, the volume history prior to measurement of compliance varied between the static and dynamic mechanical studies. Before the generation of each P-V curve, the lungs were inflated to TLC in order to provide a constant volume history and reopen closed airspaces, while Cdyn measurements were made during normal tidal breathing. This difference could account for the higher C_L values observed.

In spite of the differences between absolute values for Cdyn/kg and C_L/kg, changes in the two parameters during the first year of age closely paralleled one another. Although Cdyn/kg values did not differ statistically from one another over the age range studied, there was a trend, very similar to that of C_L/kg described in Chapter II, for smaller values in the 3-9 month old foals. This was assumed, as described in Chapter II, to result from the unequal growth of the lung compared to the rest of the body during that time period.

Although there was a slight tendency for Rpul to decrease with age (slope of allometric equation = -0.13), with the exception of the 1 year study, the values at the different ages studied were not significantly different from one another. This resulted in a marked decrease in Rpul/kg with age. In children (Cook et al., 1958) and cattle (Lekeux et al., 1983), Rpul has also been observed to decrease with the increase in lung volume and body size associated with growth. Mead (1961) suggested that this disproportionate decrease of Rpul relative to lung volume (and body size) could result from greater changes in radius relative to length or, in the case of the respiratory system specifically, greater changes in airway volume relative to lung volume.

The mechanism for the change in Rpul with age in the horse is not known, but the growth of the airways in relation to other pulmonary structures may well play an important role.

As reported in other studies of pulmonary function in the horse (Gallivan, 1981; Derksen et al., 1982) resistance measurements in the present study were characterized by considerable variability both within and between foals. Although esophageal balloon pressure has been shown in the horse to be a relatively good estimate of pleural pressure (Derksen and Robinson, 1980), problems were observed during the present series of experiments. The most obvious problem was not related to the balloon-catheter per se but rather to the behavior of the esophagus. In a number of studies in foals, particularly those 3 months of age and older, there was marked activity of the esophagus such that an almost continuous series of esophageal contractions were superimposed on the deflections associated with breathing, making the tracings virtually unreadable. Although in almost all studies, the marked contractions eventually stopped, there was still concern that variable esophageal tone influenced the esophageal pressure measured and thus influenced compliance and resistance measurements.

As expiration was consistently active, it was not possible, as it is in humans, to calculate the passive time constant of the respiratory system from the slope of the expiratory flow-volume curve. Since a difference in passive time constant has been reported between newborn and adult humans, values in infants being approximately one-half that of adults (Polgar and Weng, 1979), it was of interest to observe the changes in time constant associated with growth in the foal as well. However, it is questionable whether the product of Rpul and Cdyn (Table 3-10) as an estimate of the effective expiratory time constant is meaningful. The components of the time constant calculated were not representative of the same R and C values estimated when time constant is calculated from a flow-volume loop. My resistance values were of total pulmonary resistance, rather than of the total respiratory system resistance, and Cdyn only measured the pulmonary component of compliance instead of total respiratory compliance. In addition, in the present RC calculations, the influence of inspiration is included, while only phenomena associated with expiration should influence the slopes measured from the flow-volume loops. Therefore essentially any comparison of the RC values generated in this study with passively determined time constants in other species would probably yield meaningless results. Within the context of this study, however, RC tended to increase with age, as a result of increasing Cdyn and little change in Rpul associated with maturation.

Possible Errors and Limitations Associated with Measurement of Breathing Pattern

There is always a concern in studies which attempt to document normal behavior that the methods utilized to acquire the data do not alter the results. As was found in the adult horses, analysis of flow-volume loops generated by RIP bands with and without the facemask revealed no appreciable difference in breathing pattern between the two circumstances (Fig. 3-29). In addition, the unrestrained foal at rest could consistently be observed to contract the muscles of the abdomen phasically with expiration. Thus the facemask did not appear to alter the normal breathing pattern of the foals. Another real concern was that the foals were not sufficiently relaxed during the studies to allow measurements representative of the normal resting breathing pattern. As mentioned previously, the youngest foals adapted remarkably well to restraint and the study protocol. As the foals were studied serially over time, they grew very accustomed to the room and procedure, and were not particularly anxious. Rather, the major problem was how best to ellicit the foals' cooperation in standing quietly for a sufficient period of time. However, after some initial excitement associated with the the passage of the nasogastric tube and application of the surface electrodes, the majority of foals relaxed considerably and breathed regularly with minimum restraint. Thus, it is concluded that the breathing patterns measured in these studies are representative of a normal foal at rest.

Most of the same reservations outlined in Chapter I regarding the limitations of EMG measurement techniques apply in this study as well. In addition, the use of surface electrodes to measure Eint, and to a lesser extent Eabd, activity is also associated with certain problems. Compared to the wire electrodes, the surface leads do tend to record activity from a larger population of muscle fibers, which for this study, was desirable. However, when surface electrodes are used, it is difficult to know which muscle activity is actually being measured. For example, one cannot be certain whether the signal source is the external or internal intercostal muscle layer when using thoracic surface electrodes. In addition, signals may be referred from adjacent intercostal spaces, the diaphragm, or even the abdominal muscles. The particular location selected for placement of the Eint electrodes was an attempt to maximize the distance from potentially contaminating muscle groups. In the older foals, both inspiratory and expiratory phasic activity of the intercostal muscles were confirmed by the use of wire electrodes. In the younger foals, wire electrodes were not placed and it was assumed that thoracic surface activity was primarily from the intercostal muscles. Preliminary spectral analysis of the frequency content of the surface recordings compared to that obtained from wires indicated that it is possible that in the younger animals, the Eint signal recorded was actually a combination of signals from the diaphragm and intercostal muscles. For the purposes of this study however, which was to describe the overall breathing pattern of the growing foal, such a distinction is probably relatively unimportant.

Other problems associated with the surface electrodes were a consistently prominent cardiac artifact and a variable degree of motion artifact. In addition, it was occasionally impossible to detect phasic Eint activity because of a large amount of tonic activity. With appropriate filtering, the magnitude of both artifacts was greatly reduced, and the respiratory signal was usually sufficiently free of noise to allow easy detection of the onset of phasic EMG activity. In many studies, a larger amount of baseline noise in the Eint recordings was noted in the standing compared to the lateral position, and in some, phasic activity was totally obliterated by apparently tonic EMG activity. Often, with a shift of weight, phasic activity would again be detectable. These findings emphasize the important, and perhaps dominant role that the intercostal muscles play in maintenance of posture, as has been previously reported in the awake, unrestrained cat (Duron and Marlot, 1980).

In these studies, the role of the upper airways in determination of breathing pattern was not formally addressed. Certainly, from the observation of certain phenomena such as triple peaks of inspiration and inspiratory and expiratory obstructions, it is clear that at least under some circumstances, the muscles of the upper airways of the foal do play an important role in modulating airflow. Their relative importance in control of the overall breathing pattern of the foal has not been established. It is clear, however, that these muscles are not primarily responsible for the biphasic expiratory flow pattern observed. In awake, standing foals one month of age and less, the presence of a nasotracheal tube, which effectively circumvented the larynx, consistently prolonged T_E and actually accentuated the biphasic configuration of expiratory airflow rather than abolished it. The same was true to a lesser extent for inspiratory flow. Although considered to be an interesting observation, the determination of the mechanism responsible was considered beyond the scope of the present investigation.

Summary of the Changes in Breathing Strategy Associated With Growth in the Foal

From the results of this study, the neonatal foal was found to utilize a pattern of breathing distinct from the adult horse. Compared to the adult, this pattern was characterized by a higher frequency of breathing, higher airflow rate and minute ventilation on a body weight basis, and a primarily monophasic pattern of both inspiration and expiration. Both phases of the breathing cycle were primarily active in the foal, while in the yearling foal and adult, both inspiration and expiration were composed of both an active and passive component. Most of these findings are similar to those observed in neonates of other smaller species, and most easily explained by the need for the neonate to maintain a high ventilation because of increased metabolic requirements. This need may actually be accentuated in the foal because of high level of activity it displays from an early age. It is typical for the neonate to consistently increase the frequency of breathing in preference to tidal volume in order to achieve the high ventilation required. This has been hypothesized to be a result of an effort to minimize the work of breathing, as in neonates of other species, the work needed to overcome elastic and resistive forces has been found to be minimal at a breathing frequency of approximately 35-40 breaths per minute (Cook et al., 1957). The active expiration consistently observed in the foals is compatible with a need in the neonatal foal to maintain a high ventilation, as this would be expected to promote movement of air out of the lungs quickly. Whether other neonatal species phasically use their abdomen during expiration has not been documented.

It appears that the term neonatal foal utilizes few if any of the strategies that are thought to be used by other neonatal species to actively defend end expiratory lung volume above Vrx. In other words, in the neonatal foal, the mechanical characteristics of its respiratory system seem to influence the strategy of breathing to a lesser degree than in other neonatal species. One obvious explanation for this lies in the results of the studies of static mechanics in Chapter II. The chest wall of the neonatal foal was found to be considerably stiffer than other neonatal species, and FRC normalized to body weight or to lung volume did not change appreciably with age. These findings are in contrast to those in other neonates, in which a high chest wall compliance leads to a low Vrx and the need for active mechanisms to defend lung volume so that adequate ventilation may be maintained. It is probable that the term foal's respiratory system is sufficiently mature from a structural point of view that compensatory mechanisms to defend end-expiratory lung volume are not needed, at least in the standing position. The results from the study of breathing pattern during lateral recumbency suggest that the young foal does adopt certain breathing strategies in possible compensation for a decreased lung volume, and that vagal timing reflex activity may be important in generation of this strategy.

The final question that remains to be addressed, and probably one of the most difficult to answer, is what influences or mediates the transition from the neonatal to the adult strategy of breathing in the horse. The original hypothesis of this investigation was that this transition was primarily a result of the mechanical maturation of the respiratory system, in particular the chest wall. It was hypothesized that a substantial decrease in chest wall compliance with age could exert a sufficient effect on the mechanics of the system to induce a change in breathing pattern. In a system with a low compliance, the elastic work of breathing could be minimized by breathing substantially below Vrx, with utilization of the probably considerable elastic recoil forces of the chest wall at low lung volumes to passively inflate during the first part of inspiration. However, the time frame of change in chest wall compliance and in breathing pattern did not coincide. No further changes in chest wall compliance, normalized to body weight, were observed after the first 3 months of age. At this time, inspiration in the awake foal was consistently monophasic, and the overall breathing pattern remained quite different from that of the adult until approximately one year of age. Neither did any of the other normalized chest wall compliance values show any significant changes after the third month of age. Therefore, the hypothesis was rejected that the decrease in chest wall compliance observed with maturation was primarily responsible for the transition to a polyphasic breathing pattern.

Other mechanisms potentially influencing the transition to the adult polyphasic breathing strategy include changes in relative body proportions, changes in the relative size of abdominal contents, and simply an overall increase in size accompanying maturation. Certain changes in the relative body proportions of the growing foal were more temporally related to the transition to an adult breathing pattern than were the changes in chest wall compliance. Growth during the first 3 months of age was very rapid, with a marked increase in height and muscle mass. However, the trunk of the 3 month old foal still appeared short in relation to its height (Fig. 2-6). It was not until the foals were approximately 6 months of age that obvious growth of the trunk in both depth and length was appreciated, and this process continued through the one-year studies. The large colon of the neonatal foal also develops tremendously during the first months of life to occupy a substantial portion of the abdominal cavity, including the area in the concavity created by the dome of the diaphragm. With the development of the gastrointestinal tract and the lengthening of the trunk of the horse, it is likely that the positions of the lung fields, diaphragm, and abdominal contents all shift relative to each other. With a change to adult proportions, the lungs probably become situated progressively more dorsally to the abdominal contents. It is possible that with these changes, the orientation of the body parts change sufficiently to make a biphasic flow pattern easier or more advantageous to generate. Conclusive evidence for this hypothesis would necessitate detailed anatomical and functional investigations.

As discussed in Chapter I with respect to the adult horse, if part of the abdominal contents were located ventral to the lung fields, during inspiration, the abdominal organs should tend to fall away from the lungs. On the other hand, expiration should be facilitated by active contraction of the abdominal muscles in order to lift the abdominal viscera and overcome gravitational forces. Although the abdominal muscles were consistently active in all ages of horses studied, it is possible that their primary function changes somewhat with increasing age. In the neonate with very high metabolic requirements necessitating increased ventilation, and with a relatively small abdominal mass, expiratory muscle activity could primarily promote rapid movement of air out of the lungs. With increasing body size, however, the more important role of these muscles at rest may become overcoming gravitational forces by lifting the abdominal contents, thereby facilitating expiration. Although the exercising horse was not studied, it is possible that the airflow and respiratory muscle activation pattern of the adult horse when metabolic demands are increased may closely resemble the neonatal breathing pattern.

Important insight into the generation of the biphasic flow pattern was gained almost accidentally from observation of the pattern of tidal breathing in two foals, aged 8 days and 1 month, intubated and lightly anesthetized with pentobarbital. Tracings of the awake and anesthetized breathing patterns of both foals are presented in Fig. 3-31. It can be seen that although a typical neonatal pattern is observed in the awake state, when anesthetized, the breathing pattern became distinctly adult-like, with a biphasic inspiration and expiration, and a delay in inspiratory muscle activity (panel C). On recovery from anesthesia, the typical neonatal pattern was again adopted in both individuals. This indicates that the neural control mechanisms necessary for generation of an adult breathing pattern are present from an early age, but for some reason are usually masked in the awake neonate. This is not merely the result of an increased frequency of breathing in the awake neonate, because in many awake and anesthetized studies, a decrease in respiratory rate did not automatically result in an increase in the degree of biphasic flow pattern or in a delay of respiratory muscle activation. Rather, it probably results from some combination of most of the factors listed above, including the need for a high level of ventilation in the neonate and certain structural properties of the system, as well as a possible change in peripheral and/or central control mechanisms with maturation.

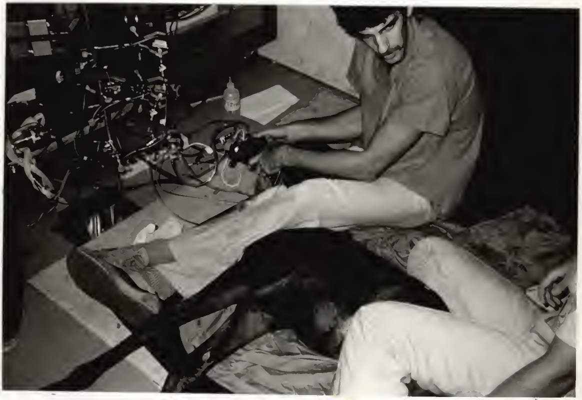


Figure 3-1. Neonatal foal restrained in lateral recumbency for measurement of ventilatory parameters with pneumotach-facemask system.

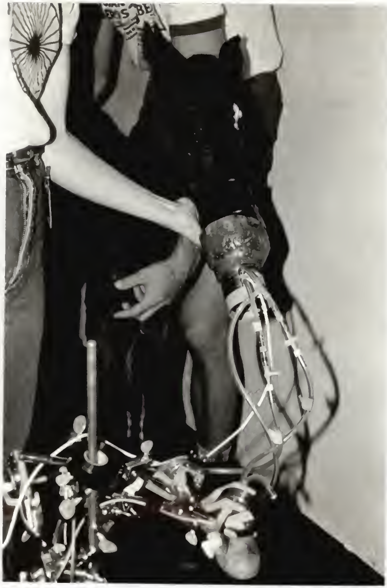


Figure 3-2. Standing neonatal foal with fiberglass facemask and pneumotach in place. Electrical tape forms an airtight seal between the mask and the foal's head.

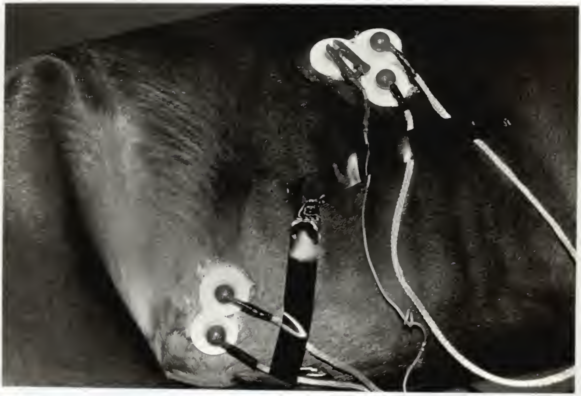


Figure 3-3. Photograph illustrating typical placement of surface EMG electrodes in a neonatal foal in lateral recumbency. Head is to right, tail to left.

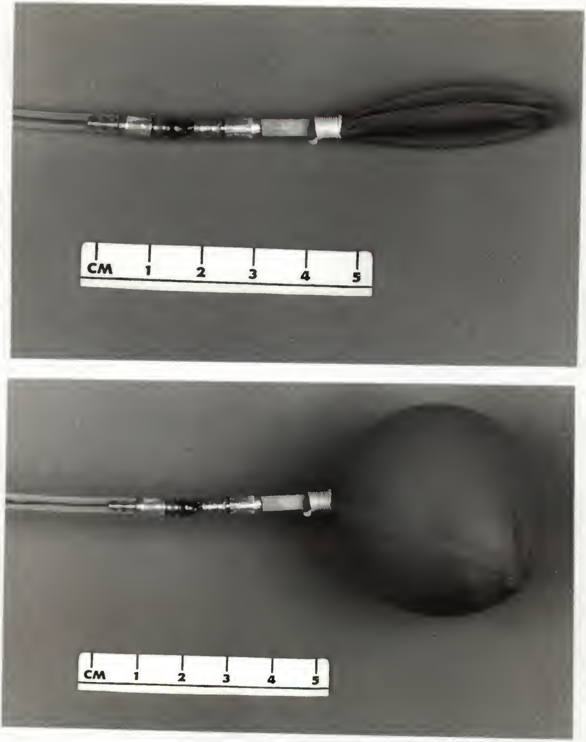


Figure 3-4. Intraesophageal bipolar silver Edi electrode used in foals during the first year of life. Inter-electrode distance has been shortened from adult version. Top panel) Balloon deflated; Bottom panel) Balloon inflated.

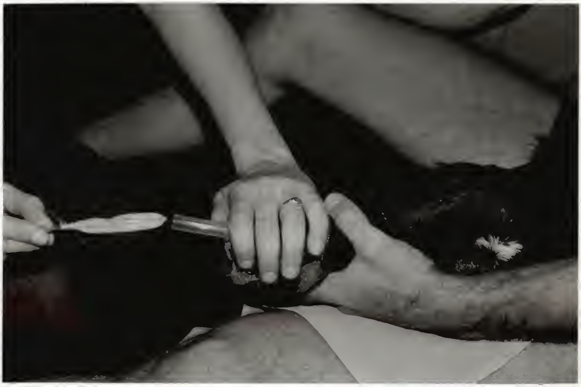
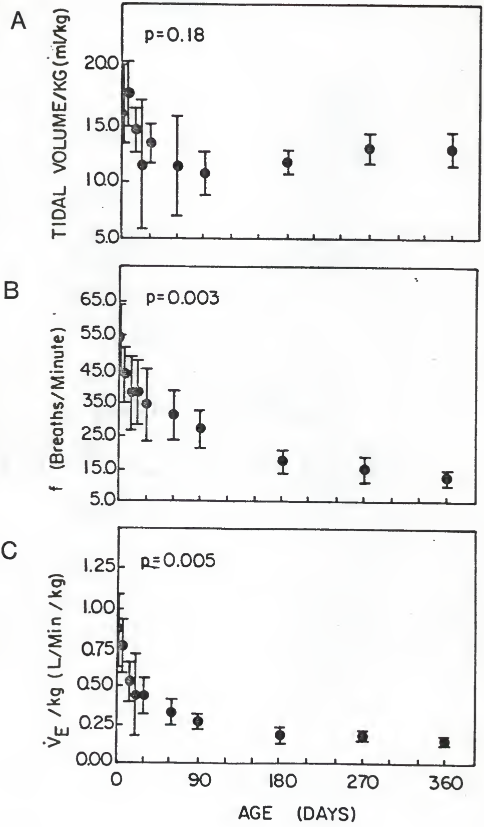


Figure 3-5. Balloon-catheter system for measurement of esophageal or gastric pressure being passed into esophagus through larger guide tube. After proper placement of balloon in caudal esophagus or stomach, the guide tube will be removed and the catheter will be secured to the foal's head.

Figure 3-6. Regression plots of ventilatory parameters in the growing foal from day 2 to 1 year of age. Solid circles represent mean values; vertical bars denote standard deviation. A) Tidal volume, normalized to body weight; B) Frequency of breathing; C) Minute ventilation, normalized to body weight. P = level of significance for slope $\neq 0$.


A
p=0.18
TIDAL VOLUME/KG (ml/kg)
20.0
15.0
10.0
5.0
B
p=0.003
f (Breaths/Minute)
65.0
55.0
45.0
35.0
25.0
15.0
5.0
C
p=0.005
$\dot{V}_E$ /kg (L/Min/kg)
1.25
1.00
0.75
0.50
0.25
0.00
0
90
180
270
360
AGE (DAYS)

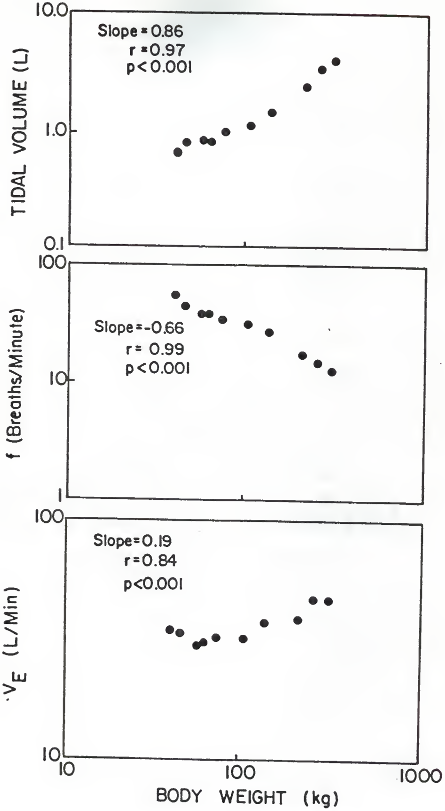


Figure 3-7. Log-log relationships between body weight (kg) and ventilatory parameters in the growing foal during the first year of life. A) Allometry of tidal volume; B) Allometry of frequency of breathing; C) Allometry of minute ventilation.

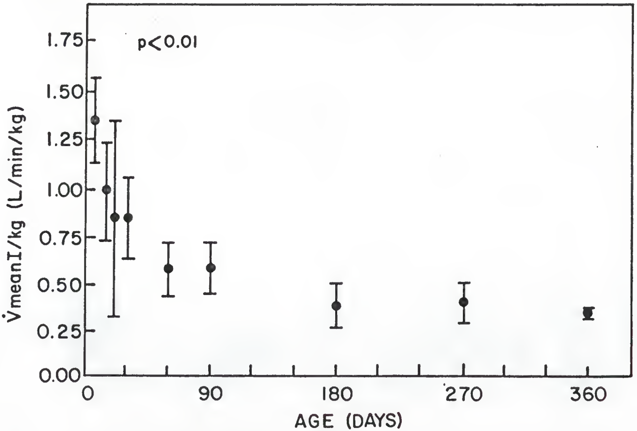
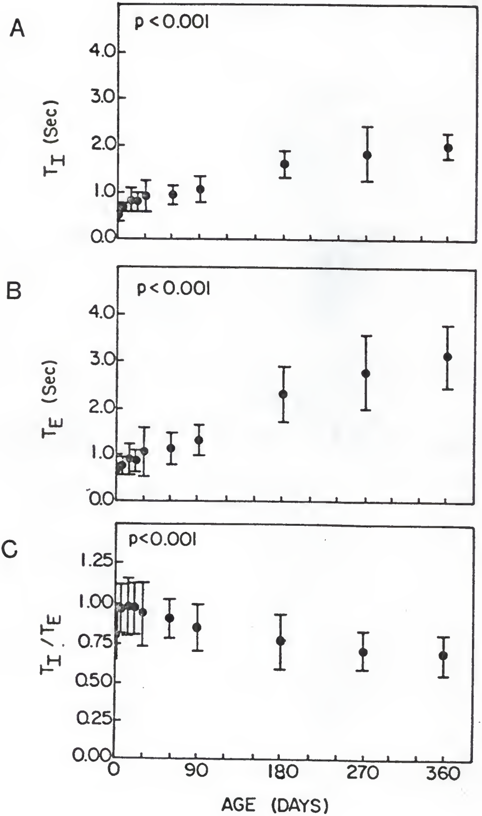


Figure 3-8. Relationship between average inspiratory airflow ($\dot{V}$meanI) normalized to body weight and age in the standing foal during the first year of life. Solid circles denote mean values; vertical bars denote standard deviation.

Figure 3-9. Timing parameters in the standing foal during the first year of life. A) Relationship between inspiratory time and age; B) Relationship between expiratory time and age; C) Relationship between ratio of inspiratory time (T_I) to expiratory time (T_E) and age. The rate of increase of T_E is greater than that of T_I, which results in a decreasing T_I/T_E ratio with increasing age. Solid circles are mean values; vertical bars represent standard deviation.


A
p < 0.001
T_I (Sec)
4.0
3.0
2.0
1.0
0.0
B
p < 0.001
T_E (Sec)
4.0
3.0
2.0
1.0
0.0
C
p<0.001
T_I / T_E
1.25
1.00
0.75
0.50
0.25
0.00
0
90
180
270
360
AGE (DAYS)

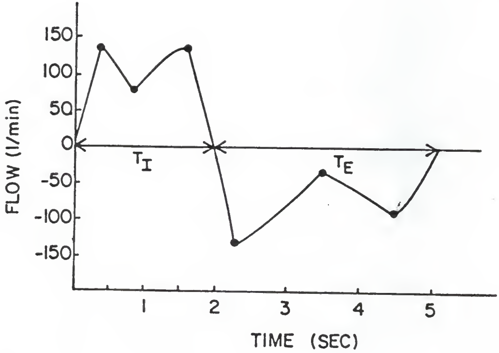


Figure 3-10. Composite breath of the 12 month old foal. Solid circles are means of peaks and dips of inspiratory and expiratory flow and the times at which they occurred. T_I is inspiratory time, T_E is expiratory time.

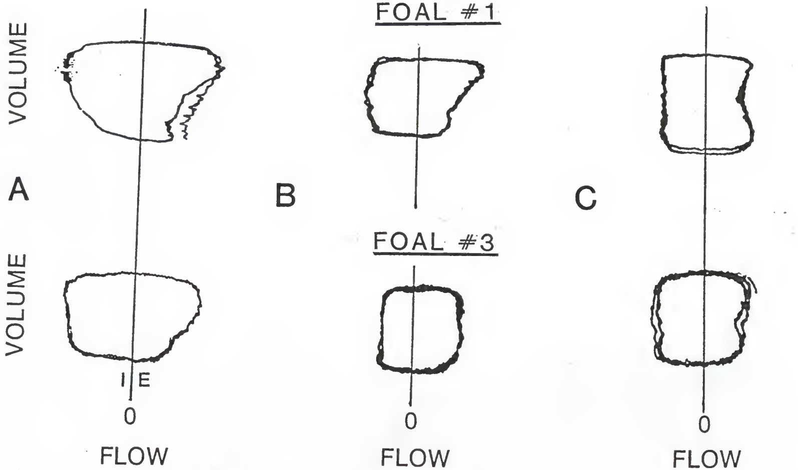


Figure 3-11. Typical flow-volume loops representing each age group studied. Across top panel are loops generated in foal #1; across bottom panel are loops obtained in foal #3. A) Loops obtained at day 2 of age; B) Week 1; C) Week 2; D) Week 3; E) Month 1; F) Month 2; G) Month 3; H) Month 6; I) Month 9; J) Month 12. All loops were obtained with foal in standing position.

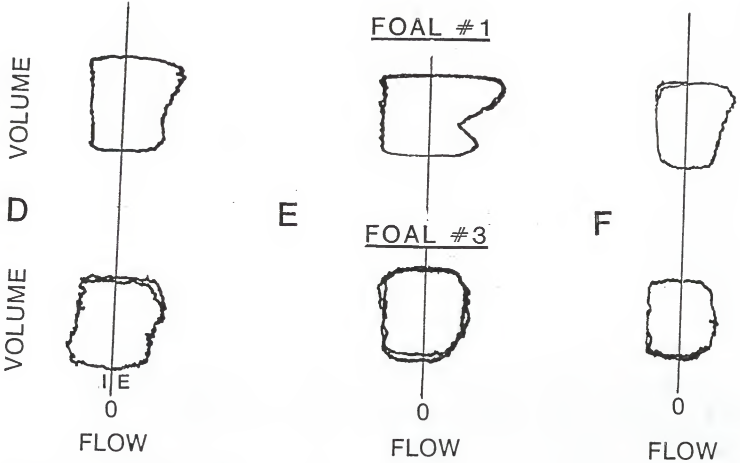


Figure 3-11. Continued.

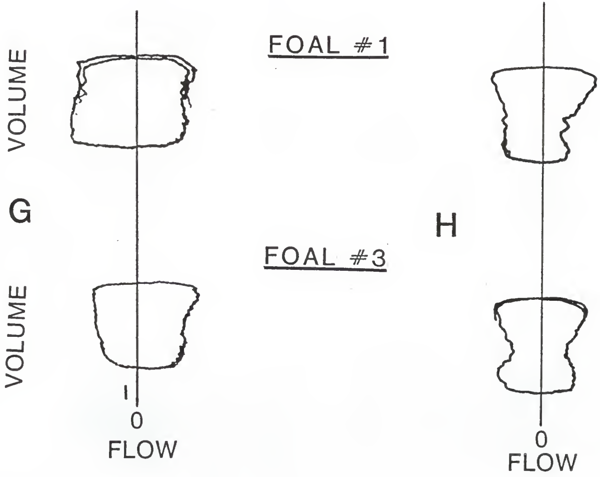


Figure 3-11. Continued.

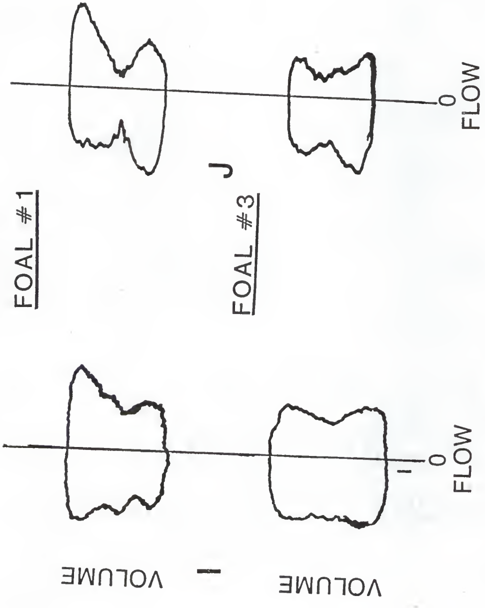
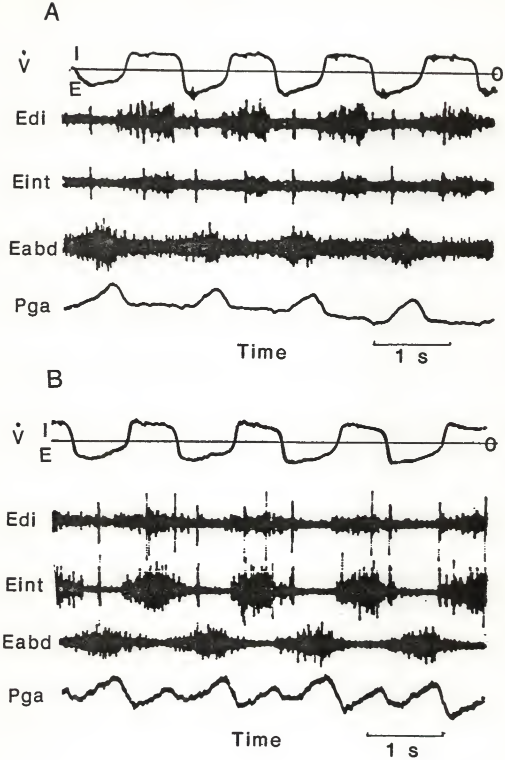


Figure 3-11. Continued.

Figure 3-12. Representative tracings of immature airflow pattern and EMG activation sequence in the young foal. Both inspiration and expiration are essentially monophasic. A) Tracings of flow ($\dot{V}$), respiratory muscle EMG activity, and gastric pressure (Pga) in a standing 6 day old foal. Onset of Edi and Eint precedes onset of inspiratory flow, and there is no detectable persistence of signal into expiration. An Eabd signal is present during expiration, and Pga peaks toward the end of expiration. B) Same parameters as in A, recorded in another 6 day old foal, showing similar trends to those described above. Both Eint and Eabd persist slightly into the following expiration or inspiration. C) Flow-volume loop in a 3 week old standing foal, showing monophasic inspiration and slightly biphasic expiration. D) Same breath represented by paintbrush flow-volume loop, showing Edi activity through majority of inspiration.


A
V̇
I
E
0
Edi
Eint
Eabd
Pga
Time
1 s
B
V̇
I
E
0
Edi
Eint
Eabd
Pga
Time
1 s

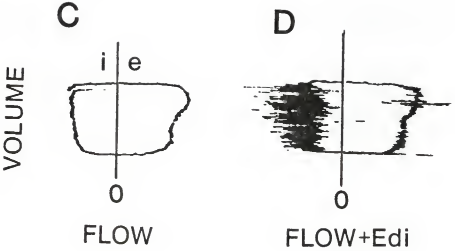
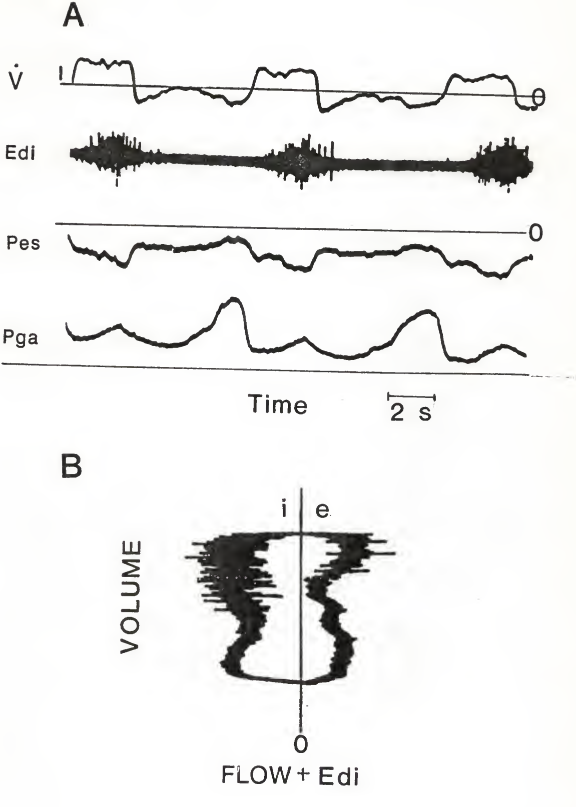


Figure 3-12. Continued.

Figure 3-13. Representative tracings of mature, adult-like flow ($\dot{V}$), pressure and EMG activation pattern in a 12 month old foal. Note obvious biphasic inspiration and expiration, and pronounced delay in onset of Edi activity relative to onset of inspiratory flow. A) Flow, Edi, and pressure tracings against time; B) Paintbrush flow-volume loop of breath #2 from above tracing, illustrating passive and active component of inspiration.


A
V̇
0
Edi
Pes
0
Pga
Time
2 s
B
i
e
VOLUME
0
FLOW + Edi

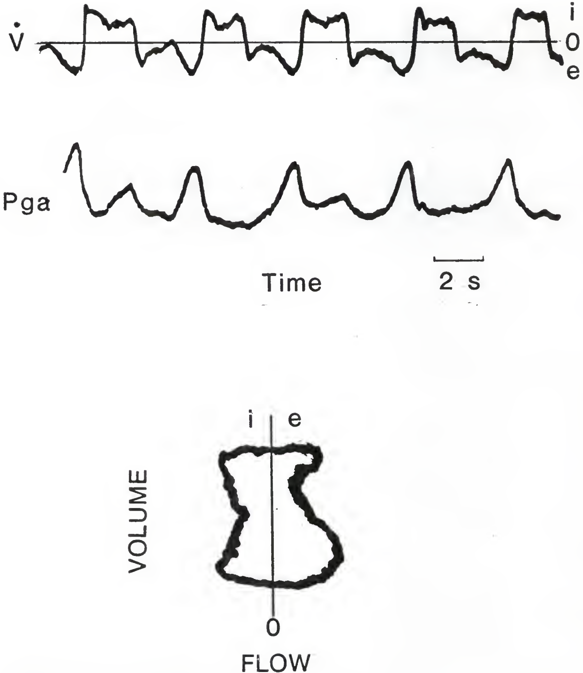
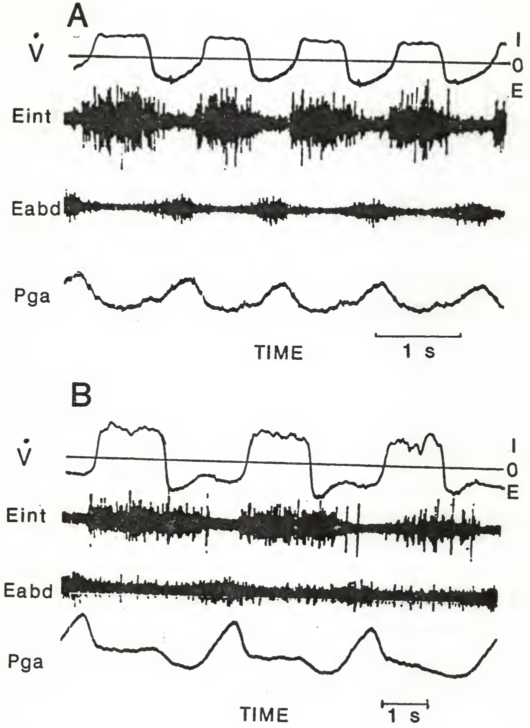


Figure 3-14. Representative breaths obtained in a 1 month old foal (#8), demonstrating obvious biphasic inspiration and expiration. Onset of Edi slightly lagged onset of inspiratory flow in some breaths. Top panel) Flow and gastric pressure tracings plotted against time; Bottom panel) Flow-volume plot of breath #3.

Figure 3-15. Representative tracings of flow ($\dot{V}$), Eint, Eabd, and gastric pressure (Pga), plotted against time in 2 standing foals. In both panels, (A and B), Eint is markedly persistent into expiration. A) Tracing obtained in a 2 week old foal, showing monophasic flow pattern, early onset of Eint activity relative to onset of inspiratory flow, and the presence of Eabd activity from early expiration. B) Tracing obtained from a 7 month old foal, showing a more biphasic expiration and inspiration, with most of Eabd activity observed during the second part of expiration.


A
$\dot{V}$
I
0
E
Eint
Eabd
Pga
TIME
1 s
B
$\dot{V}$
I
0
E
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Eabd
Pga
TIME
1 s

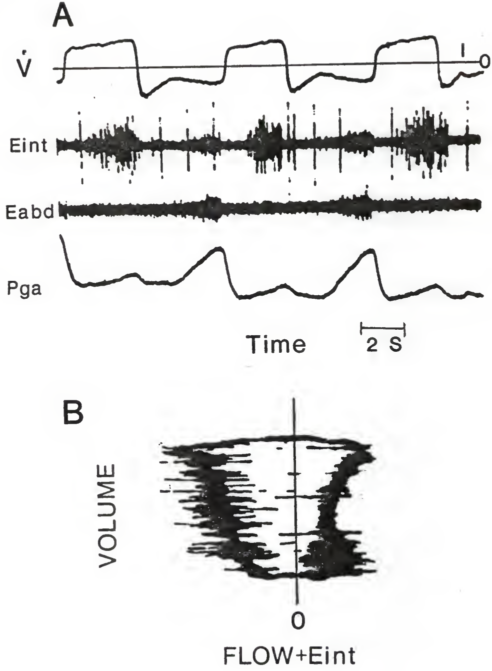


Figure 3-16. Representative tracings of flow ($\dot{V}$), volume, Eint, Eabd, and gastric pressure in a 9 month old foal (#1). The Eint recordings, obtained using surface electrodes, show both inspiratory and expiratory activity. In plots against time (A), and in flow-volume diagrams (B), it is clear that Eint activity occurs primarily during the latter portion of both inspiration and expiration.

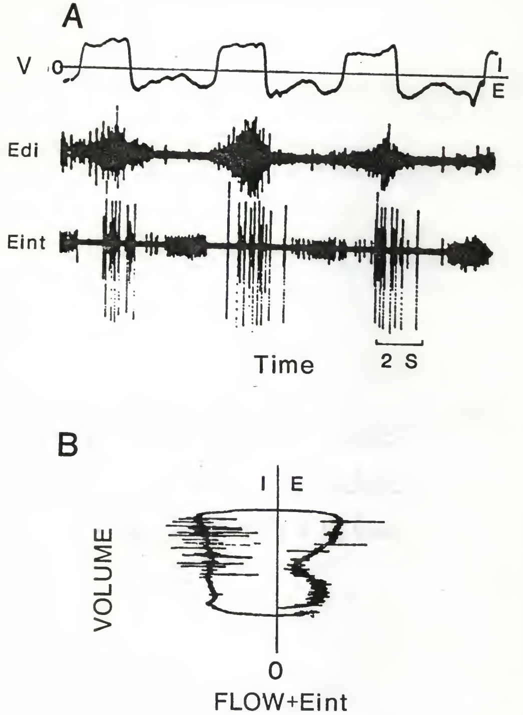


Figure 3-17. Tracings of flow ($\dot{V}$), Eint, and Edi obtained in a standing 1 year old foal (#1). The Eint recordings were obtained using fine wire intramuscular electrodes. Inspiratory and expiratory Eint activity is obvious during the second part of both inspiration and expiration. A) Tracings against time; B) Flow-volume diagram, with Eint added to flow.

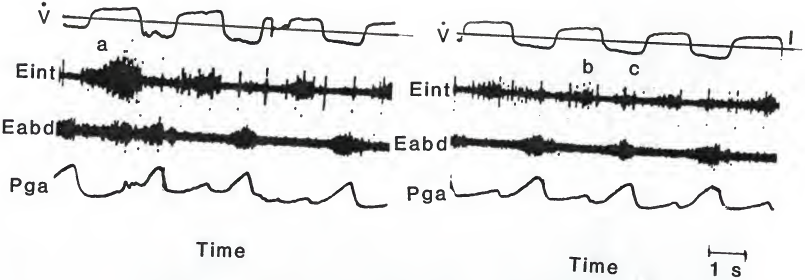


Figure 3-18. Continuous tracings of flow ($\dot{V}$), Eint, Eabd, and gastric pressure in a 3 month old standing foal, showing 2 patterns of Eint activity. a) Onset of Eint activity preceds onset of inspiratory flow, and no expiratory Eint activity is apparent. In the following breaths, the onset of inspiratory Eint activity (b) shortly lags the onset of inspiratory flow and expiratory Eint activity becomes apparent (c).

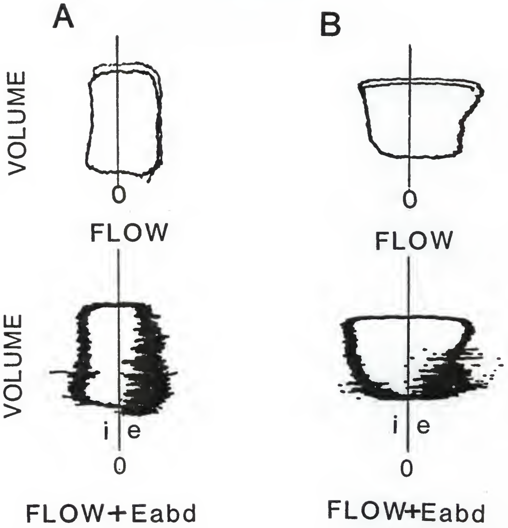


Figure 3-19. Paintbrush flow-volume diagrams with Eabd added to flow signal. A) Top panel: Showing box-like, monophasic expiratory flow pattern in a 1 week old foal; Bottom panel: Showing paintbrush flow-volume loop of same breath, Eabd activity is apparent throughout expiration. B) Top panel: Flow-volume loop obtained from 3 month old foal, with more pronounced biphasic flow pattern; Bottom panel: When Eabd added to flow signal, delay in onset of Eabd relative to onset of expiratory flow is apparent.

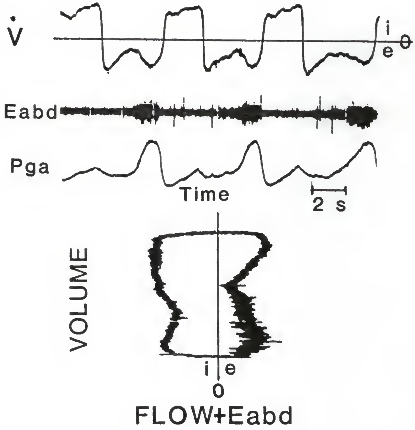


Figure 3-20. Representative tracings of an adult-like expiratory flow pattern in a 1 year old foal. In both the tracings against time and the flow-volume diagram, a markedly biphasic expiratory flow pattern is obvious, with delay in activation of abdominal muscles until flow reaches close to zero. Expiration is clearly composed of both an active and passive component.

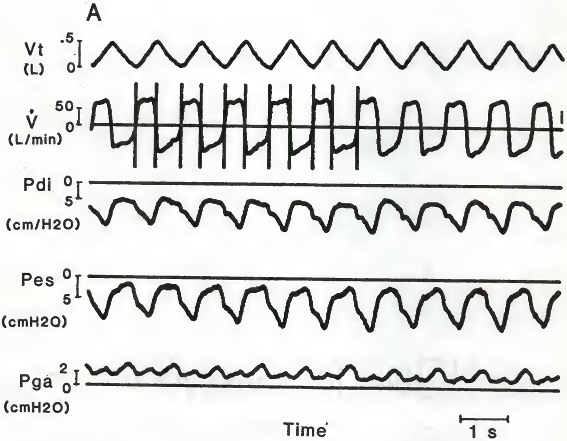


Figure 3-21. Representative digitized tracings from standing foals of tidal volume (Vt), flow (V̇), transdiaphragmatic pressure (Pdi), esophageal pressure (Pes), and gastric pressure (Pga) for different age groups studied. A) Day 2, foal #3; B) Day 6, foal #4; C) Week 2, foal #3; D) Week 3, foal #2; E) Month 1, foal #1; F) Month 1, foal #2; G) Month 2, foal #1; H) Month 3, foal #5; I) Month 3, foal #1; J) Month 6, foal #1; K) Month 9, foal #4; L) Month 12, foal #5. Panel J, point A shows onset of decline of Pdi is closely associated with onset of inspiratory flow. Panel L, point B shows that onset of decline of Pdi during inspiration is more closely associated with the low point in inspiratory flow. Vertical lines on flow tracing represent points of zero flow.

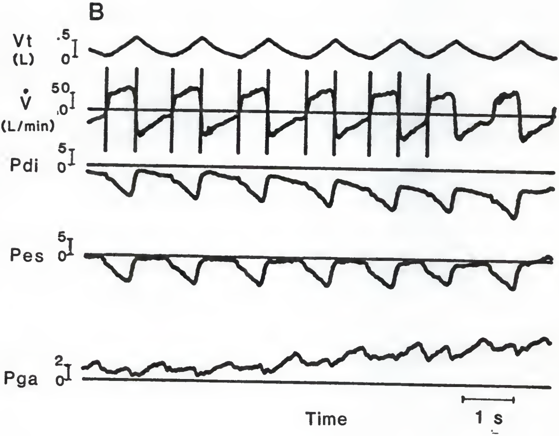


Figure 3-21. Continued.

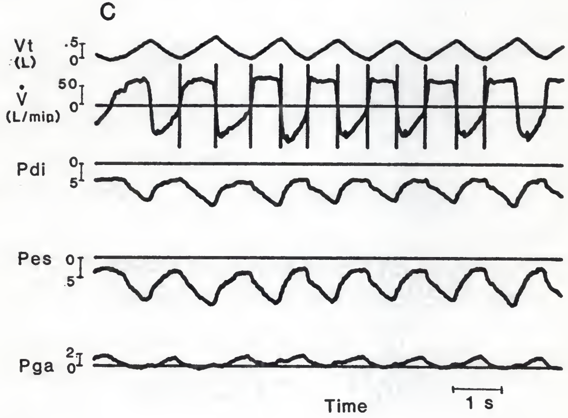


Figure 3-21. Continued.

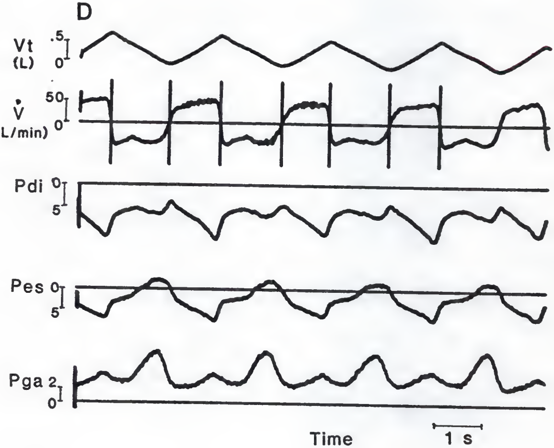


Figure 3-21. Continued.

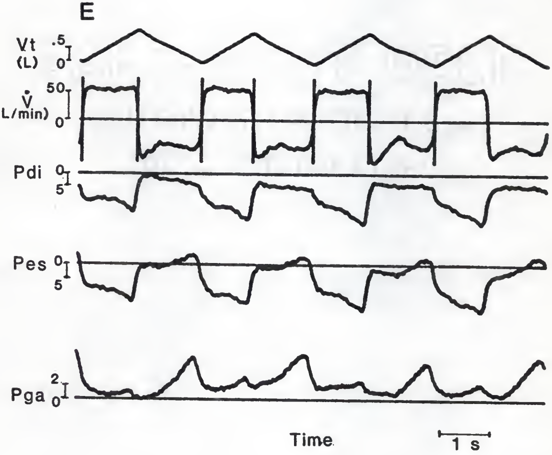


Figure 3-21. Continued.

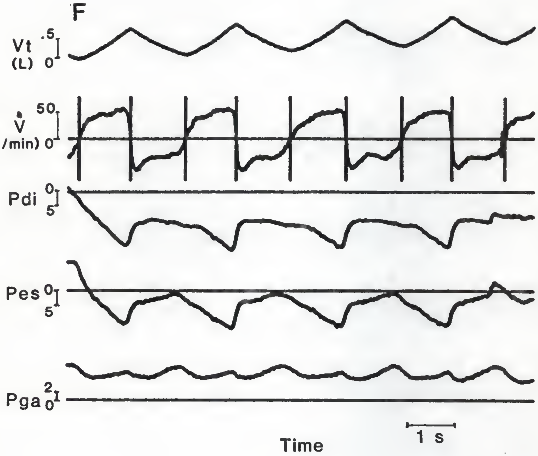


Figure 3-21. Continued.

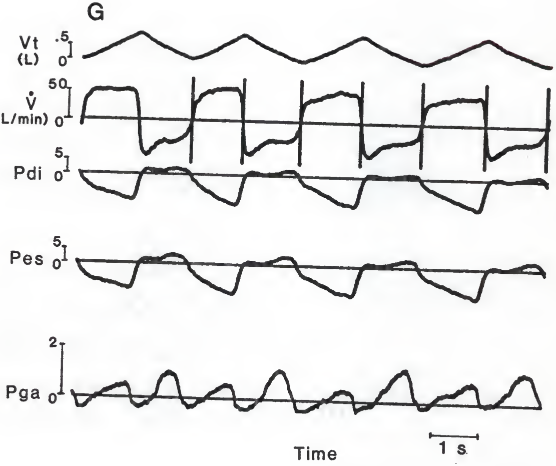


Figure 3-21. Continued.

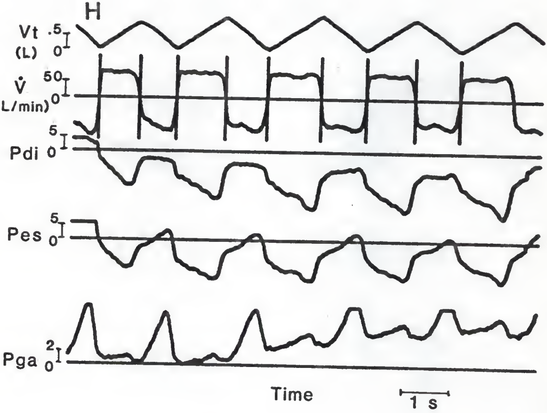


Figure 3-21. Continued.

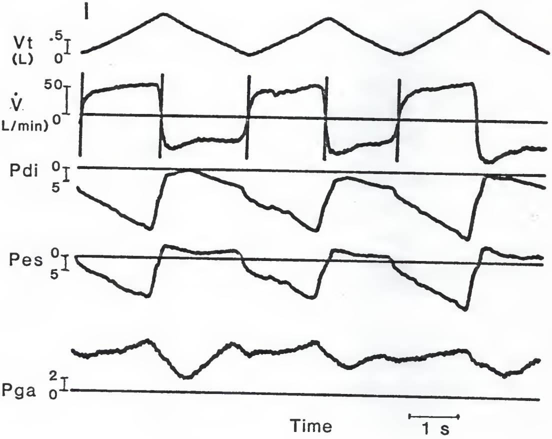


Figure 3-21. Continued.

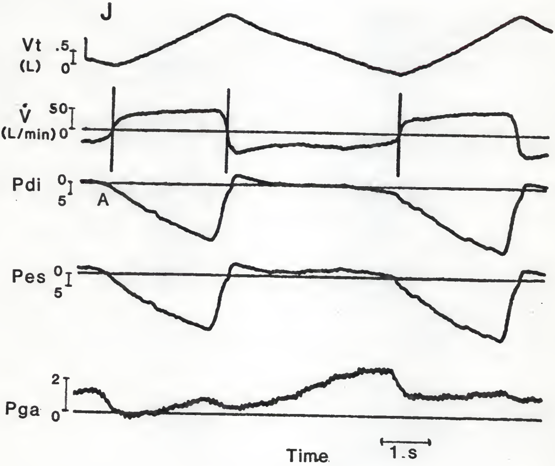


Figure 3-21. Continued.

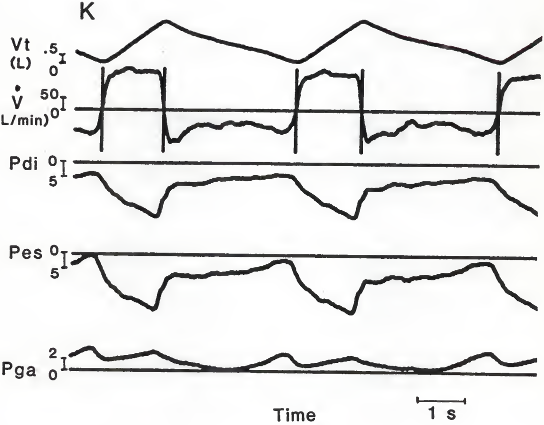


Figure 3-21. Continued.

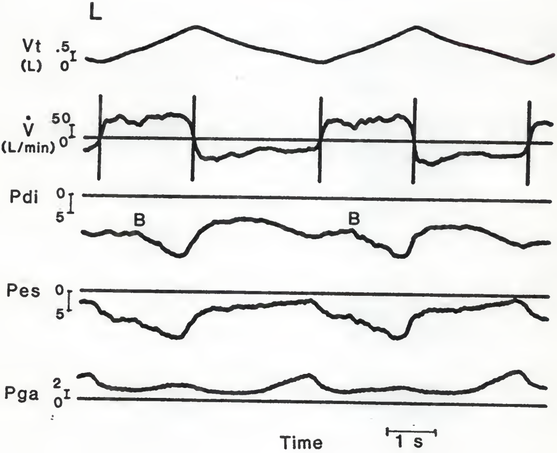


Figure 3-21. Continued.

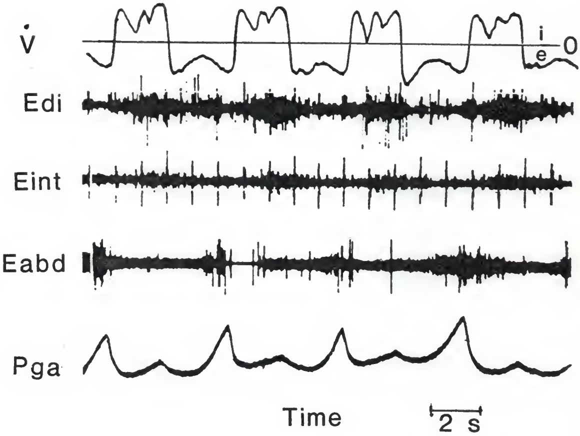


Figure 3-22. Flow and EMG tracings generated in a 12 month old foal, demonstrating triple peaks of inspiratory flow with biphasic expiration. As is evident in breath #3 above, Edi tracings often showed several bursts of activity during inspiration when triple flow peaks were evdent.

Figure 3-23. Flow and EMG tracings of a sigh followed by an apneic pause in a 12 month old standing foal. A) Tracing of sigh against time; B) Expanded time scale of same breath. In panel B, the sigh is accompanied by Edi activity persistent well into expiration. During the ensuing apneic pause, a small burst of Edi activity can be observed, with no visible effect on the flow tracing. This suggests that the apnea was obstructive in nature. In addition, prominent Eabd activity with a concurrent rise in Pga during the apnea indicates that the respiratory muscles were not relaxed during the pause.

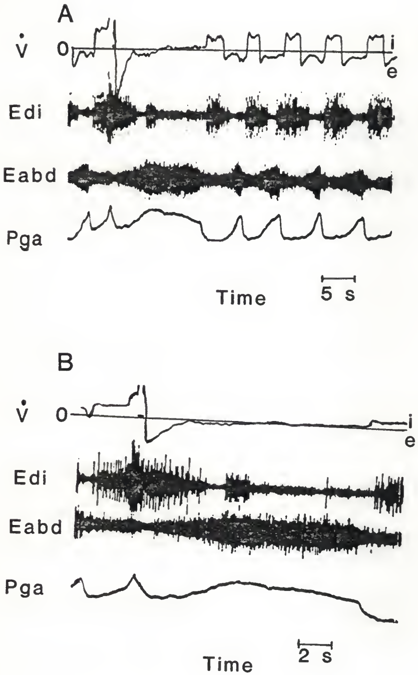
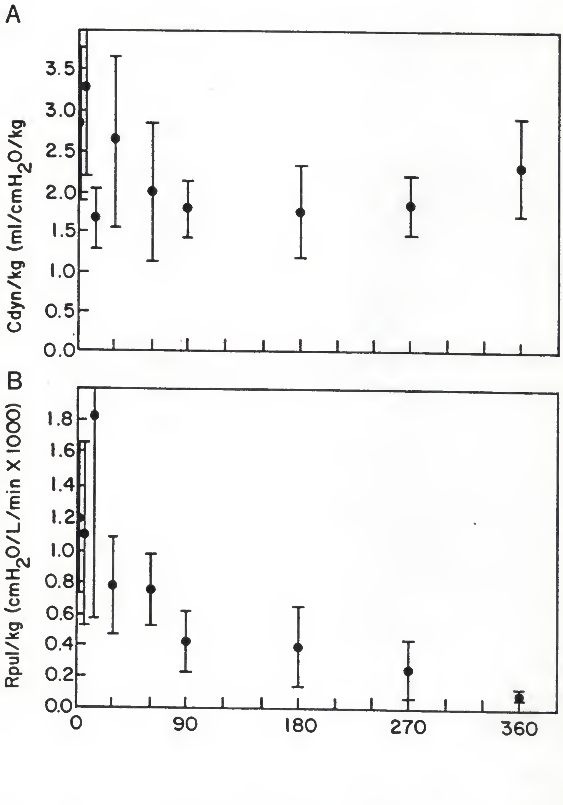

A
$\dot{V}$
0
i
e
Edi
Eabd
Pga
Time
5 s
B
$\dot{V}$
0
i
e
Edi
Eabd
Pga
Time
2 s

Figure 3-24. Dynamic compliance normalized to body weight (A), and total pulmonary resistance normalized to body weight (B), in the awake, standing foal during the first year of life. Solid circles represent mean values, vertical bars denote standard deviation.


A
Cdyn/kg (ml/cmH2O/kg
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
B
Rpul/kg (cmH2O/L/min X 1000)
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
1.6
1.8
0
90
180
270
360

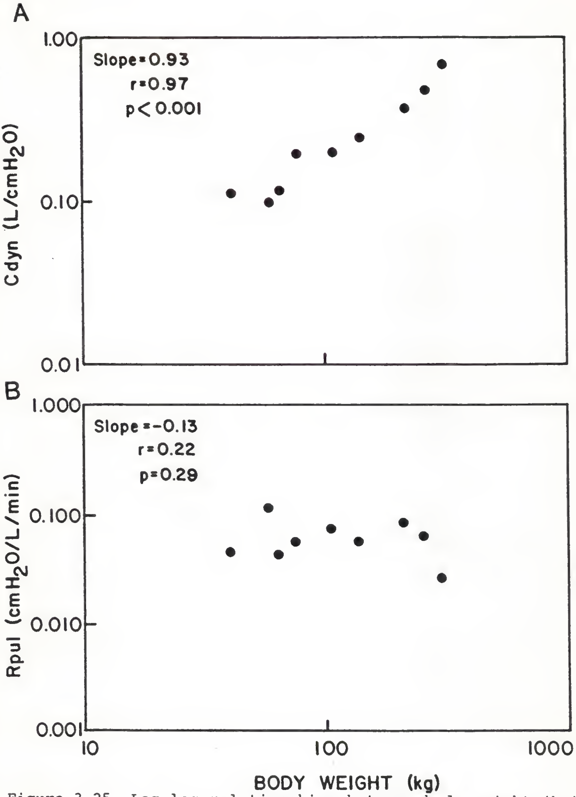
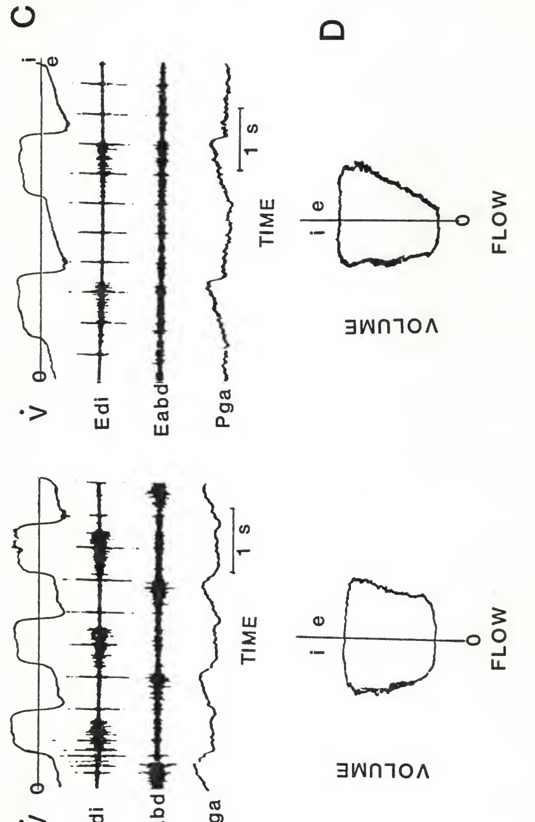


Figure 3-25. Log-log relationships between body weight (kg) and compliance and resistance measurements in the standing foal during the first year of life. A) Allometry of dynamic compliance; B) Allometry of total pulmonary resistance.

Figure 3-26. Tracings illustrating two patterns of breathing in lateral recumbency, obtained in a 3 week old foal. A) Flow, EMG, and Pga tracings against time. Edi activity ends prior to the end of inspiratory flow, and Eabd activity is present during expiration, accompanied by an increase in Pga; B) Flow-volume loop of breath #3, showing a very slightly biphasic expiratory flow pattern. C) Flow, EMG, and Pga tracings in the same foal a short time later. Eabd activity is absent, and no rise is observed in Pga during expiration. Expiratory flow shows an exponential decrease compatible with a passive process. D) Flow-volume diagram of breath #1. Linear configuration of expiratory limb is supportive of passive expiration, in the absence of Eabd activity.


A
V̇
i
e
Edi
Eabd
Pga
TIME
1 s
B
VOLUME
FLOW
0
C
D

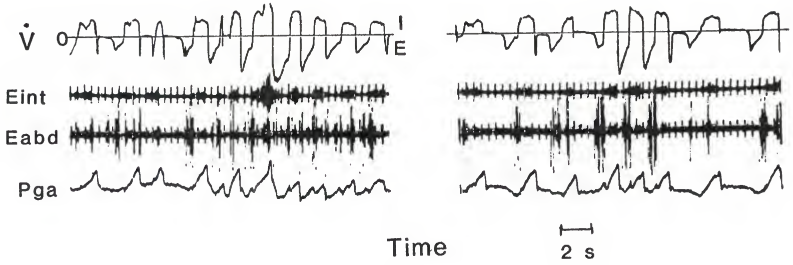


Figure 3-27. Tracings of V, EMGs, and Pga against time during sleep in a laterally recumbent 2 week old foal. Note number of inspiratory and expiratory obstructions and marked variability in airflow rate and frequency of breathing.

Figure 3-28. Tracings illustrating typical patterns of expiratory obstructions in the laterally recumbent foal. A) Tracings of flow, EMGs, and Pga against time in a 1 month old foal. Edi is persistent through the first part of expiration. Concurrent with the release of the upper airway obstruction, Eabd activity is observed, resulting in a peak of Pga near the end of expiration; B) Tracings of same parameters against time in a laterally recumbent 3 week old foal. Edi is not persistent into expiration. No Eabd activity or increase in Pga is observed with the release of the upper airway obstruction.

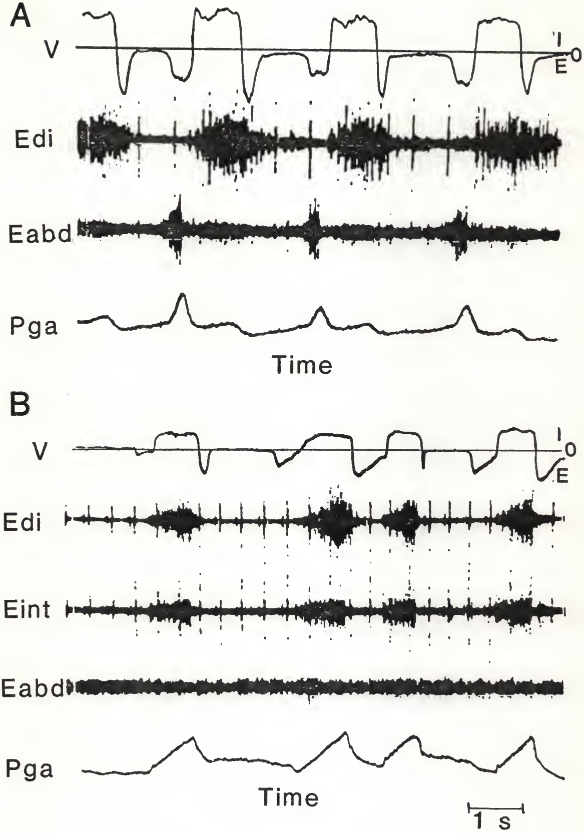

A
V
I
0
E
Edi
Eabd
Pga
Time
B
V
I
0
E
Edi
Eint
Eabd
Pga
Time
1 s

Figure 3-29. Pneumotach and RIP generated flow-volume loops in the foal. The top two rows, breaths #1-4, compare loops generated by the pneumotach to those of the same breath obtained using respibands, in different aged foals. Bottom row shows loops generated using respibands without facemask in place. Biphasic expiration is obvious, with and without facemask.

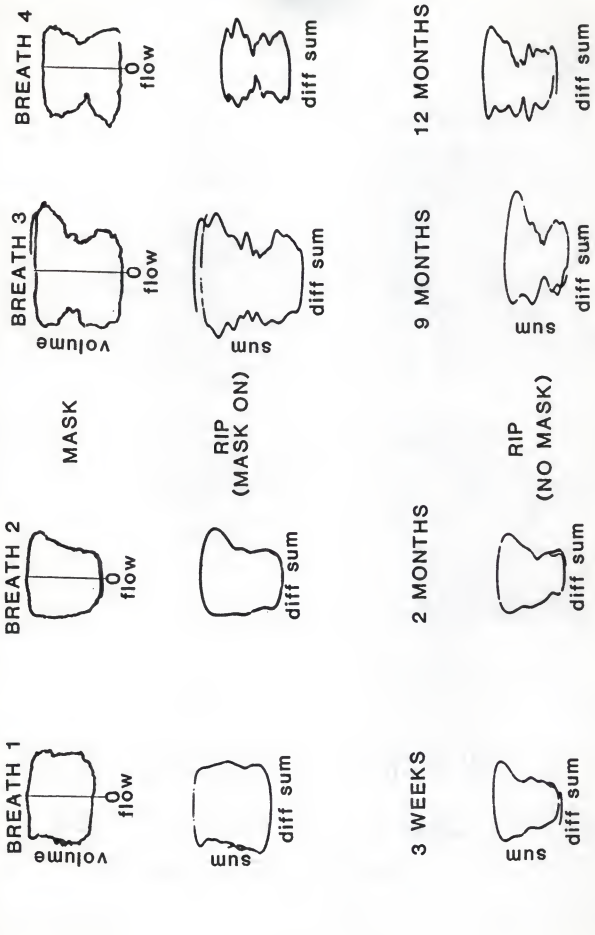

BREATH 1
volume
0
flow
BREATH 2
0
flow
MASK
BREATH 3
volume
0
flow
BREATH 4
0
flow
sum
diff sum
diff sum
RIP
(MASK ON)
sum
diff sum
diff sum
3 WEEKS
2 MONTHS
9 MONTHS
12 MONTHS
sum
diff sum
diff sum
RIP
(NO MASK)
sum
diff sum
diff sum

Figure 3-30. Tracings of tidal breathing in two 2 week old foals. A) Flow-volume loops of same breath obtained from standing foal. To right, paintbrush flow-volume loop showing Eabd activity through the majority of expiration. Without the EMG data, the configuration of the loop suggest that expiration was interrupted before passive deflation to Vrx was completed, and that EEV was greater than Vrx. B) Tracings acquired from foal in lateral recumbency. From the linear configuration of the expiratory limb of the flow-volume loop, in the absence of the EMG data, it would have been concluded that expiration was passive. However, from the rise of Pga and Eabd activity associated with expiration, it is clear that expiration was, in fact, active.

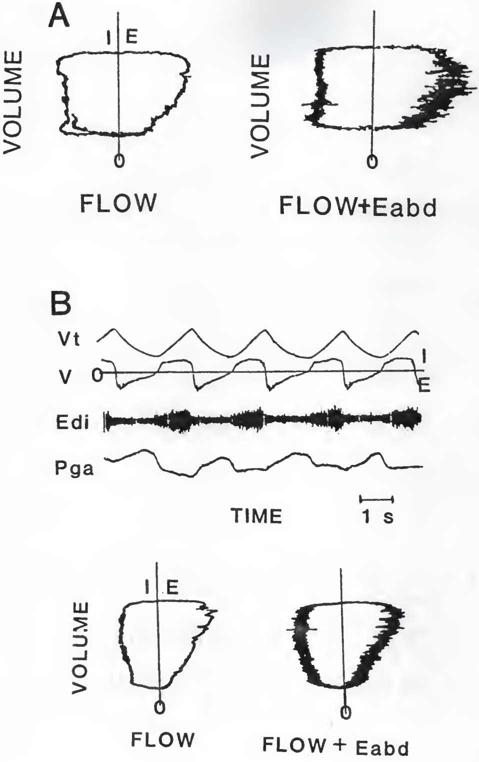
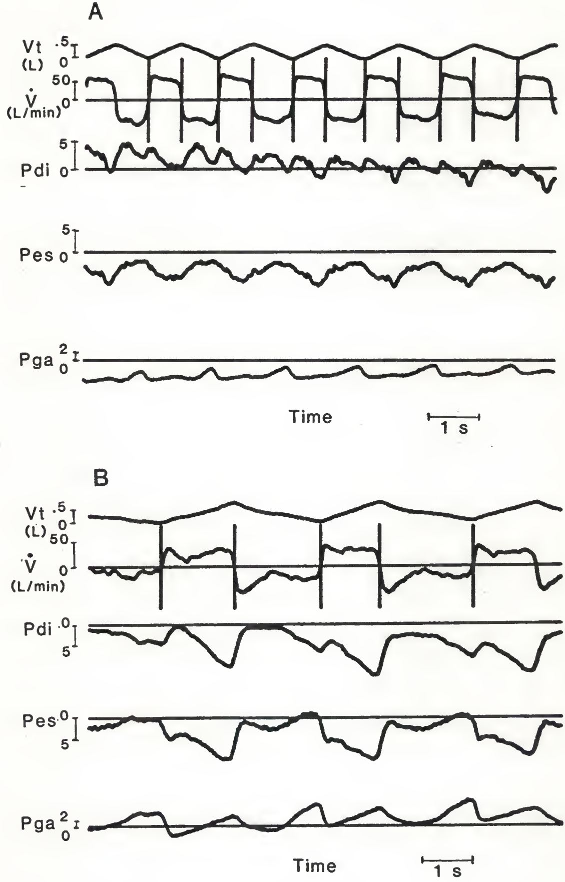

A
VOLUME
I
E
0
FLOW
VOLUME
0
FLOW+Eabd
B
Vt
V
0
I
E
Edi
Pga
TIME
1 s
VOLUME
I
E
0
FLOW
0
FLOW + Eabd

Figure 3-31. Representative tracings from 9 day old foal (A and B) and 1 month old foal (C). A) Tracings acquired during awake breathing in standing position. Note essentially monophasic inspiration and expiration; B) Same parameters measured in same foal under pentobarbital anesthesia while maintained in sternal recumbency. Typical adult pattern of breathing can be observed, consisting of markedly biphasic inspiration and expiration, and an increasing Pdi during the first part of inspiration; C) Left panel: Awake tidal breathing in a 1 month old foal, exhibiting monophasic inspiration and expiration; Right panel: Same foal under anesthesia. Tracings of flow, EMGs, and Pga against time and flow-volume diagram. Note delay in activation of Eint relatve to onset of inspiratory flow and more pronounced biphasic component to both inspiration and expiration.


A
Vt (L)
.5
0
50
V̇ (L/min)
0
5
Pdi
0
5
Pes
0
2
Pga
0
Time
1 s
B
Vt (L)
.5
0
50
V̇ (L/min)
0
Pdi
.0
5
Pes
0
5
Pga
2
0
Time
1 s

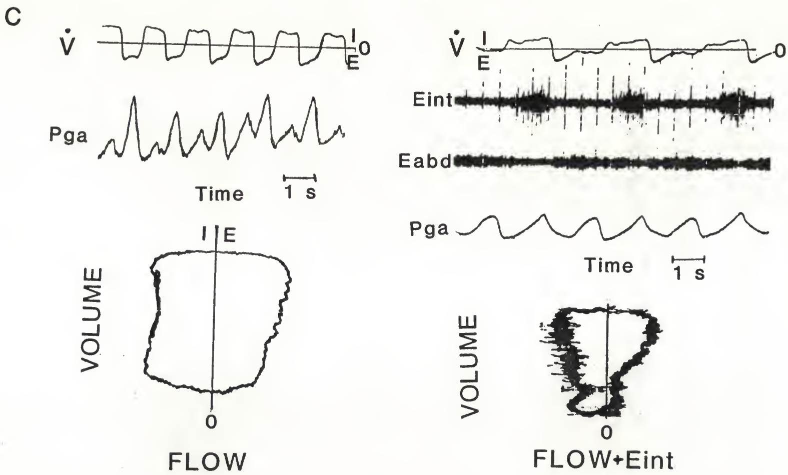


Figure 3-31. Continued.

GENERAL CONCLUSIONS

In this study of developmental changes in breathing strategy in the growing horse, four hypotheses were tested. First, it was hypothesized that the polyphasic airflow pattern utilized by the adult horse at rest resulted from a respiratory muscle activation pattern that allowed the horse to breathe around, rather than from the relaxation volume of the respiratory system. This hypothesis is accepted based on airflow, respiratory muscle EMG and pressure data generated in a group of adult horses (Chapter I). The biphasic inspiratory and expiratory airflow pattern previously reported by other authors was confirmed in all horses studied. From the EMG data, it was shown that there was an active and passive component to both inspiration and expiration secondary to a delay in activation of both inspiratory and expiratory muscle groups relative to onset of airflow. After a period of passive deflation during the first part of expiration, activation of the abdominal muscles during the second part of expiration was responsible for the second peak of inspiratory flow and deflation to an end-expiratory lung volume (EEV) less than Vrx. From this low EEV, passive inflation occurred toward Vrx, utilizing the energy stored during the previous active expiration.

This was followed by active inspiration, resulting from both diaphragmatic and intercostal muscle contraction. Measurements of Pga and Pdi during the breathing cycle were consistent with the respiratory muscle activation pattern. Therefore, the expiratory muscles share with the inspiratory muscles the work of breathing, and generate a pattern of breathing in which end-expiratory volume is substantially less than Vrx. By breathing around Vrx, the adult horse at rest may minimize the work of breathing.

The second hypothesis consisted of two separate, but related components. First, it was hypothesized that the mechanical characteristics of the respiratory system of the neonatal foal are similar to those of other neonatal species. More specifically, a compliant chest wall is a structural requirement of all neonatal species, but predisposes to a low Vrx, which may interfer with gas exchange and the efficiency of ventilation in the neonatal foal. Second, because of these structural characteristics, the neonatal foal, like other species of newborn mammals, adopts a breathing strategy different from that of the adult in order to actively maintain EEV above Vrx. The present studies confirms the hypothesis that the neonatal breathing pattern in the awake foal differs from that of the adult horse. In regard to ventilatory parameters, the frequency of breathing was considerably higher in the newborn foal, while tidal volume on a body weight basis was similar to the adult value, resulting in a much higher minute ventilation (normalized to body weight) than the adult. The neonatal foal achieved this high ventilation by the use of an essentially monophasic flow pattern. In contrast to the adult, during inspiration, diaphragmatic activation consistently preceded the onset of inspiratory flow, and abdominal muscle EMG (Eabd) activity was detectable during the majority of expiration, rather than during late expiration, as typically observed in the adults. Thus, both inspiration and expiration in the young foal were primarily active events. Although Eabd activity was detectable in every standing foal, abdominal efforts usually resulted in a less pronounced biphasic expiratory flow pattern compared to the adult.

Because of the presence of active expiration and a monophasic flow pattern, it was very difficult to determine the exact postion of Vrx relative to EEV during awake breathing in the neonatal foal. The hypothesis that the foal routinely breathes from above Vrx, in order to defend lung volume, was rejected for several reasons. Little evidence was found to suggest that mechanisms were utilized to retard expiratory airflow. Persistent post-inspiratory inspiratory muscle activity was observed considerably less frequently in the young foals than in the adult horses. Use of the abdomen through most of expiration would be expected to enhance, rather than retard expiratory airflow, and thus aid in rapid deflation of the lungs to a low lung volume. Although activity of upper airway muscles was not specifically studied, the configuration of the flow-volume loops typically was not consistent with expiratory braking or obstruction. Limited evidence suggests that EEV was actually somewhat less than Vrx, but not to the extent that was observed in adult horses.

The static mechanical properties of the respiratory system of the foal did in some ways resemble those of other neonatal species. Residual volume was determined by airway closure instead of the elastic recoil of the chest wall, lung compliance appeared to be slightly decreased in the youngest age group of foals, and the unstressed position of the chest wall decreased with maturation. However, the chest wall of the foal was found to be considerably stiffer than that of any other neonatal species previously studied. In addition, FRC/kg and FRC/TLC remained constant with increasing age, as did lung recoil pressure at FRC (PtpFRC). From these findings, it is probable that the respiratory system of the neonatal foal is sufficiently mature from a structural standpoint that compensatory mechanisms to defend end-expiratory lung volume are not needed. Therefore, although the neonatal chest wall was found to be considerably more compliant than the yearling foal chest wall, no evidence was found to support the hypothesis that Vrx was decreased in the neonatal foal because of an immature chest wall.

The third hypothesis that the transition between the neonatal and adult pattern of breathing is completed within the first year of life is accepted. In terms of ventilatory parameters, f, Vt/kg, and $\dot{V}_E$/kg had all reached adult values by one year of age. Absolute lung volumes, flow rates, and dynamic compliance values in the yearling foal were still substantially lower than adult values because the overall body size of the yearling was less than of the adult horse. Maturation from the neonatal to adult breathing pattern appeared to involve a delay in activation of both inspiratory and expiratory muscle groups, which established a passive and active component to both inspiration and expiration. Throughout the study period, concurrent with the increase in delay of abdominal EMG activation, the expiratory flow pattern became progressively more biphasic in appearance. The time of appearance of a consistent biphasic inspiratory flow pattern was considerably later, at approximately one year of age, and coincided with the appearance of a delay in diaphragmatic activation relative to inspiratory flow. The striking similarity between the composite breaths obtained from the group of adult horses and from the yearling foals together with the EMG and pressure data strongly suggest that the adult breathing pattern is achieved by one year of age.

The fourth hypothesis, that the change in breathing strategy observed during the first year of life is a result primarily of the mechanical maturation of the chest wall, is rejected because the timing of changes in breathing pattern did not coincide well with changes in chest wall compliance.

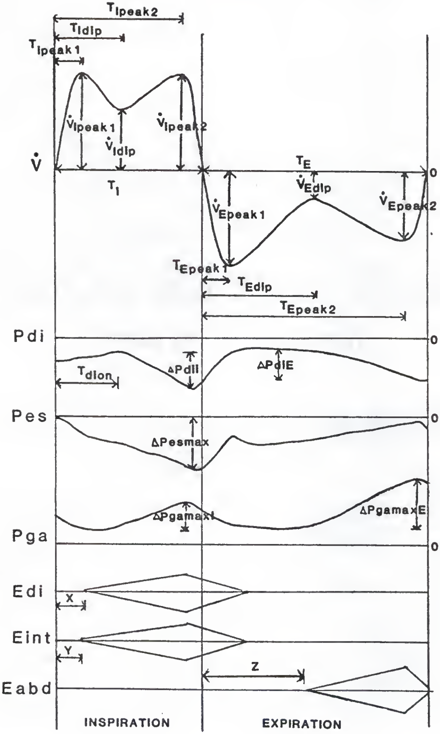
Chest wall compliance normalized to body weight did decrease substantially during the first 3 months of age, but after this time, no further changes were noted. At this age, although expiration was more obviously biphasic than in the neonatal foal, the overall breathing pattern remained considerably different than that of the adult. Inspiration was consistently monophasic, there was no delay in inspiratory muscle activation relative to onset of inspiratory flow, and breathing frequency was still elevated above adult values.

Although a decrease in chest wall compliance was rejected as the primary mechanism influencing the transition to the polyphasic breathing pattern, a more viable explanation was not conclusively identified. From observations of spontaneous breathing in lightly anesthetized neonatal foals, it was established that from an early age, the foal is able to generate an adult pattern of breathing, but for some reason(s), this pattern is usually masked in the awake state. Alternate explanations for the transition in breathing strategy include change in body proportions and/or body size with growth and maturation of central and peripheral respiratory control mechanisms. Additional studies to further address this question could examine the relative importance of peripheral neural feedback mechanisms in generation of breathing pattern in different ages of foals.

In these studies, in the process of addressing the specific hypotheses proposed, several more general observations were made regarding developmental respiratory physiology. First, during analysis of the static mechanical data in particular, it became obvious that growth of the respiratory system during the first year of life was dysanaptic in nature. The increase in lung volumes appeared to lag the growth of other body structures, such as muscle and bone, during the first few months of age when increases in overall body size were most rapid. This resulted in a lower ratio of lung volume/kg in these age groups. However, with the development of a longer, deeper trunk and a slower rate of growth of the legs, the normalized lung volumes started to increase toward more adult-like proportions, as observed in the 6 to 12 month old foals. It would be of interest to determine the pattern of growth of the respiratory system during the completion of the growth process in the horse. Second, several of the results of this study reinforce the idea that it is unwise to make extrapolations from results generated in one species of newborn animal and apply them to another. In particular, there is a wide range of maturity across neonatal species, and structural and functional characteristics of a small immature neonate may be very different than those in a large, precocious newborn such as the foal. As a result, the pattern and time frame of growth of an organ system in a neonate relatively mature at birth may differ considerably from those less mature. It is clear, however, that although the foal is considerably more mature than many other neonates at birth, a definite transition is still made from the neonatal to adult respiratory system.

APPENDIX
SCHEMATIC DIAGRAM OF REPRESENTATIVE TIDAL BREATH OF ADULT HORSE

Figure A1. Schematic diagram of tidal breath plotted against time, of adult horse, illustrating biphasic inspiratory and expiratory flow pattern. $\dot{V}$ = airflow, Pdi = transdiaphragmatic pressure, Pes = esophageal pressure, Pga = gastric pressure, Edi = diaphragm EMG, Eint = intercostal EMG, Eabd = abdominal muscle EMG. Other abbreviations are listed in Key to Symbols. Vertical lines represent points of zero flow. X = difference between onset of inspiratory flow and onset of diaphragm EMG, Y = difference between onset of inspiratory flow and onset of Eint, Z = difference between onset of expiratory flow and onset of Eabd activity. Tdion = difference between onset of inspiratory flow and time at which Pdi begins its descent or changes slope of descent.


T_{Ipeak2}
T_{Idip}
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$\dot{V}_{Edip}$
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$\dot{V}_{Epeak1}$
$\dot{V}_{Epeak2}$
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T_{Edip}
T_{Epeak2}
Pdi
0
ΔPdiI
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Pes
0
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ΔPgamaxI
ΔPgamaxE
Pga
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Edi
X
Eint
Y
Z
Eabd
INSPIRATION
EXPIRATION

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I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

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